Human Research Program
Human Health Countermeasures Element

Evidence Book

Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity

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Astronauts' physical performance during a mission, including activity in microgravity and fractional gravity, is critical to mission success. Setting minimum fitness standards and measuring whether crew can maintain these standards will document the effectiveness of maintenance regimens.

I. Executive Summary

Maintenance of aerobic capacity during and after space flight is a significant concern to NASA. There is evidence that aerobic capacity is maintained during short-duration space flight, but that maximal exercise performance is impaired after landing, perhaps due to the combined effects of orthostatic stress and relative hypovolemia. Recent data from International Space Station (ISS) crewmembers participating in long-duration missions demonstrates that their heart rate responses to standard submaximal exercise intensities is increased, suggesting their aerobic capacity is decreased, although this has not been directly measured. Decreased aerobic capacity during space flight is related to concomitant reductions in physical activity, plasma volume, erythrocyte mass, and muscle conditioning. Ground-based experiences with the bed rest analog support the concept that prolonged unloading, combined with reduced levels of activity, results in decreased aerobic capacity, but the development of successful exercise countermeasures is possible. Mission success during longer microgravity exposures, prolonged lunar habitation, and Mars exploration missions may be directly impacted by decreased aerobic capacity, manifested as decreased tolerance to extended work activities and the inability to respond with sufficient reserves to the high energy demands of emergency or off-nominal tasks. Specifically during lunar and Mars exploration, crews may be tasked to perform prolonged daily extravehicular activity (EVA), and in order to successfully complete these tasks, countermeasures to protect aerobic capacity will be necessary.

II. Introduction

A reduction in aerobic capacity will cause a diminished capacity to perform strenuous physical tasks. With regard to space flight applications, aerobic capacity impacts the ability to perform an egress task while wearing the required space suit during launch and landing (15); therefore, a decreased aerobic capacity may represent a safety concern in the event of an emergency, especially immediately after landing. During lunar EVAs conducted during the Apollo era, there are several reports of EVA intensity becoming high, usually manifested by heart rates reaching 150-160 beats•min^{-1} (138). These heart rates are equivalent to approximately 78–85% of maximum heart rate (HRmax). It is not certain that aerobic capacity was reduced during the Apollo flights; nevertheless, it appears that lunar EVAs may have at times required high work outputs which taxed the aerobic exercise capacity of the crews.

The gold standard measure of aerobic capacity is maximum oxygen uptake (VO_2max), which is directly related to the physical working capacity of an individual (5;8). VO_2max is the maximal level of oxygen utilization that can be attained during exercise requiring a large muscle mass (114). Delivery of oxygen to the active muscles involves cardiac output (Q_c) and extraction of oxygen by the muscles measured as arterial-venous (a-v) oxygen difference. The relationship between VO_2, Q_c and a-v O_2 difference is described by the Fick equation (142):

$$VO_2 = Q_c \times (a\text{-}v)O_2 \text{ difference}$$

Expressed for VO_2max, the equation becomes:

$$VO_2max = Q_cmax \times max(a\text{-}v)O_2 \text{ difference}$$

Q_c is the product of heart rate (HR) and stroke volume (SV, the volume of blood ejected from the left ventricle per beat). Thus, the Fick equation can be written as:

$$VO_2 = HR \times SV \times (a\text{-}v)O_2 \text{ difference}$$

Any factor which influences maximum HR, SV or $(a\text{-}v)O_2$ difference may influence VO_2max, particularly if it cannot be compensated by one of the other contributing factors. For example, if SV has declined, HR might increase to compensate. However, the range of compensation may be limited; for example, HR can only increase a finite amount (that is, to an individual's HRmax).

Exposure to microgravity causes rapid changes in submaximal exercise responses and a decline in aerobic exercise capacity (28;63). Crewmembers who participate in short (111;121) and long-duration space flight (118) can maintain or even improve in-flight exercise response by performing in-flight exercise countermeasures, but postflight performance under the influence of gravity or orthostatic stress is not well protected. Levine et al. (111) found that Space Shuttle crewmembers participating in flights of 9 and 14 days experienced no significant decrease in aerobic capacity during their mission, but VO_2max was reduced by 22% immediately post flight. A study of this type has not been repeated for long-duration space flight. Results from long-duration in-flight *submaximal* exercise tests suggest that aerobic capacity is near preflight levels at the end of the mission (97); however, aerobic capacity as estimated by the HR response to submaximal exercise is reduced by 19% five days after landing (120). Current operational limitations prohibit VO_2max testing on landing day; thus the extent of the decrement on the most provocative mission day is unknown and is not likely to be determined in the near future.

Maintenance of upright exercise capacity after space flight – whether in full or partial gravity – is operationally important to the success of a mission and perhaps to crew survival (104;184). For example, crewmembers may be required to perform an emergency egress from the Space Shuttle. Emergency egress represents a significant metabolic (>2.5 $l \cdot min^{-1}$) and cardiovascular (>160 $beats \cdot min^{-1}$) stress in normal ambulatory subjects (15) and would be a much greater challenge after long-duration ISS missions that typically last 6 months or more. Mission requirements during lunar and Mars exploration missions have not been well defined or characterized, but we expect that the deconditioning effects of partial- and micro-gravity exposure will impact task performance.

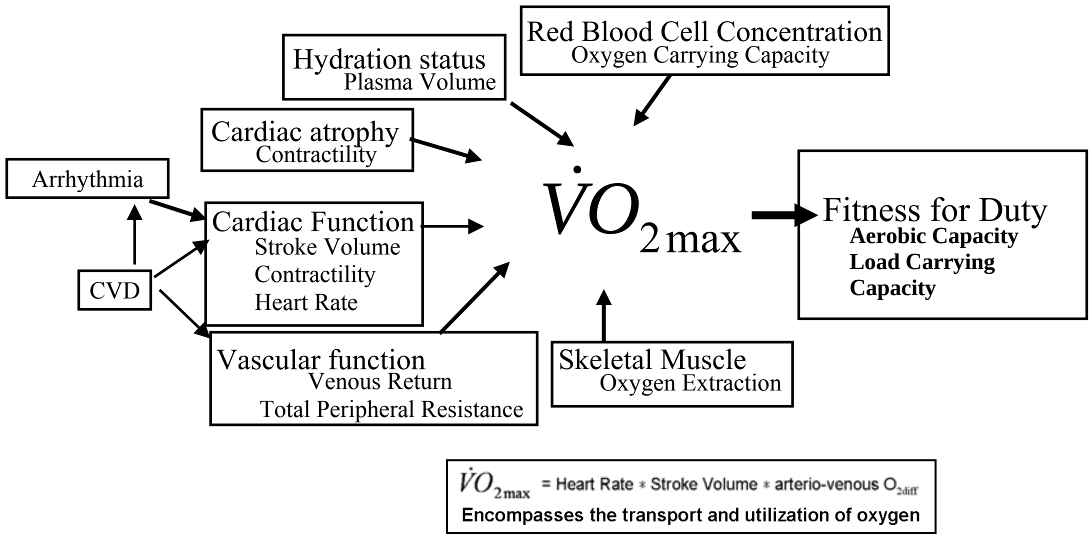

Figure 1. Diagram showing the major physiological contributors to VO_2max.

Many physiological factors influence aerobic capacity (**Figure 1**). The most rapidly occurring adaptation to space flight and bed rest, which appears to have a strong influence upon aerobic capacity, is plasma volume. In a review of previous investigations, Convertino (31) reported that 70% of the variability in VO_2max following bed rest deconditioning can be explained by a decreased plasma volume. Similarly, Stegemann et al. (168) reported that decreased blood volumes were related to a decreased aerobic capacity after space flight. Reduced circulating plasma volume may negatively affect exercise SV, the delivery of oxygen and nutrients to working muscle, and the removal of metabolic waste products. A reduced plasma volume is even more problematic during upright (rather than supine) exercise post-bed rest because of a possible increased pooling of blood in the abdomen and lower body with gravitational stress, thus further compromising exercise cardiovascular response.

With exposures of at least 6 weeks to simulated microgravity (bed rest), structural changes in the myocardium (135) and the vasculature (195) may increasingly impair the delivery of oxygen to working muscles. Additionally, negative metabolic adaptations to simulated microgravity, such as reduced citrate synthase activity, become apparent after 4 weeks of unloading (10;81). Citrate synthase is a rate limiting enzyme in the Krebs cycle; therefore, it plays a critical role in aerobic metabolism at the cellular level. Longer durations of space flight are associated with decreased muscle mass, strength, and endurance which would be expected to impair aerobic exercise performance and decrease the efficacy of the muscle pump to protect venous return (193).

III. Evidence

A. Spaceflight

Most of the observations regarding aerobic capacity during and after space flight reviewed in this section are derived from experiences in the U.S. space program. Most space flight studies have used the HR response to submaximal exercise loads to make assumptions about changes in aerobic capacity. This practice is based upon the general observation in ground-based studies that subjects will have a higher HR at a given absolute exercise intensity when they are not well-conditioned compared to the HR that would be observed following exercise training. However, as discussed below, this method of determining changes in aerobic fitness has limitations that may lead to erroneous conclusions regarding changes in VO_2max. Unfortunately, there have been few studies in either the U.S. or Russian programs that have actually measured VO_2max during or following space flight, and these studies were conducted on short-duration (less than 14 days) space flight participants.

1. Project Mercury

The success of the sub-orbital flight of Alan B. Shepard in the Mercury space capsule "Freedom 7" on May 5, 1961, marked the beginning of manned exploration of space by the U.S. Project Mercury was conducted using small vehicles capable of holding only one occupant. These early flights were conducted to orbit a manned spacecraft around the earth, to investigate man's ability to function in space, and to demonstrate the successful recovery of both man and spacecraft safely. During the six flights of the Mercury program, two suborbital and four orbital, no studies of aerobic capacity were conducted. During the orbital flights, however, exercise tests were conducted in the space craft. Crewmembers performed a 30-second exercise session using a bungee cord with a 16-pound pull through a distance of 6 inches (189). The crewmembers' HRs were increased during exercise and rapidly recovered afterwards. These were the first demonstrations that the cardiovascular system is reactive to exercise during space flight.

Although exercise intolerance was not observed, in-flight exercise training was recommended for crewmember protection during future space flight missions. Specifically, the following quote was included in the post-mission report of the third U.S. manned orbital flight (13):

> "An orthostatic rise in heart rate, fall in systolic blood pressure, and maintenance of the diastolic pressure was noted during the 24 hours immediately after landing. Such a hemodynamic phenomenon may have more serious implications for a longer mission. A prescribed in-flight exercise program may be necessary to preclude symptoms in case of the need for an emergency egress soon after landing."

This statement indicates that exercise was being considered by NASA as a possible countermeasure for space flight exposure as early as 1962.

2. Project Gemini

The Gemini project was conducted from 1964-1966 using two-man space capsules launched to orbit atop modified U.S. Air Force Titan-II intercontinental ballistic missiles. These flights were conducted to gain experience necessary to conduct future missions to the moon. Therefore, the objectives of these flights were to subject man and equipment to the space flight environment for periods lasting up to 2 weeks, to practice docking and rendezvous with orbiting target vehicles, and to refine the landing methodology. There were 12 Gemini flights: 2 unmanned and 10 flights with 2-person crews.

During three of the manned flights (Gemini IV-4 days, Gemini V-7 days, and Gemini VII-14 days), exercise testing was conducted as part of an experiment designated as

M003 – Inflight Exercise and Work Tolerance (12). These tests consisted of crewmembers performing 30 second exercise sessions with a bungee pull device (**Figure 2**). The target rate of pulling was one pull per second and the device delivered a force of 70 lbs (31.8 kg) at full extension. Heart rate and blood pressure were measured during these tests, which were conducted several times during each of the missions.

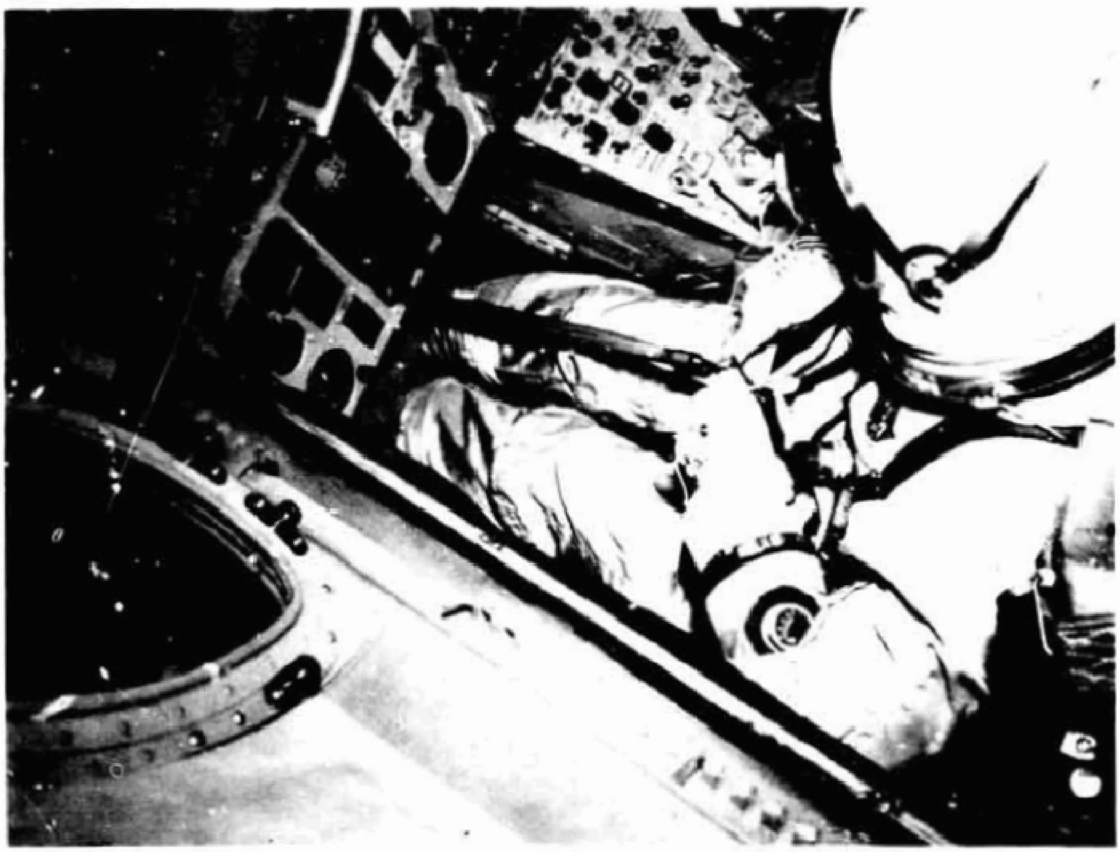

Figure 2. Gemini in-flight exerciser from Dietlein and Rapp, 1966. (48).

The HR response of the crewmembers to the brief exercise session remained relatively constant within an individual throughout the flights (**Figure 3;**(48)). The investigators suggested that these results indicated there were no decrements in the physical condition of the crews during flights of up to 14 days. The workloads imposed by this test were relatively mild and the testing time duration was brief, therefore, it is likely this test was not a specific or sensitive measure of aerobic capacity.

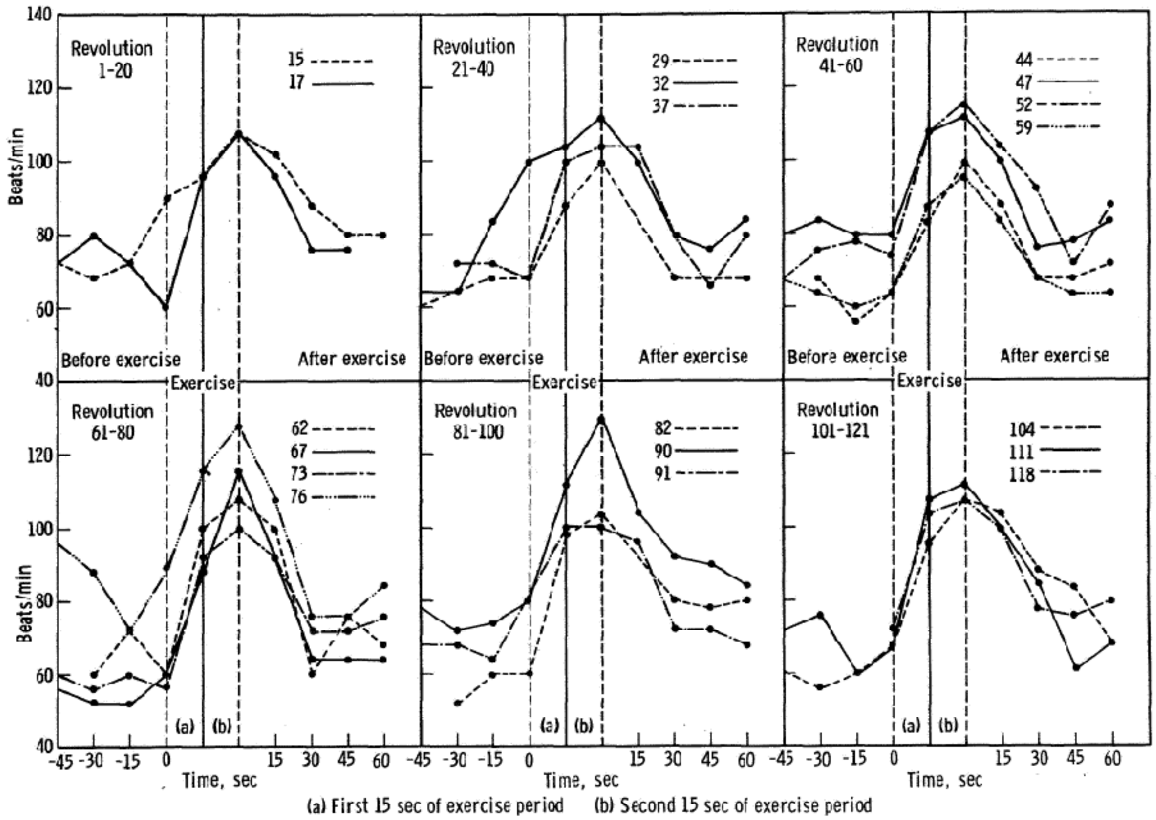

Figure 3. Example of Gemini inflight exerciser heart rate data from a single crewmember (from Barry and Catterson, 1967 (12).

Additionally, the first preflight and postflight graded exercise tests were performed by six crewmembers from four of the Gemini flights to determine the effects of microgravity on postflight performance (12;48). The test protocol was conducted on an electronic cycle ergometer on which the crewmember pedaled at 60-70 rpm. The work rate was set initially at 50 Watts for 3 minutes and increased by 15 Watts each minute until the crewmember's HR reached 180 beats·min^{-1}. The data from these tests were never published in a comprehensive fashion, but in the NASA Gemini Summary Conference Report (12) it was reported that all but one of the crewmembers tested experienced a decrease in exercise capacity. Decline in exercise capacity was demonstrated by an increase in the HR response to exercise and a reduction in oxygen consumption at exercise termination. For example, the oxygen consumption at test termination was 19 and 26% lower after flight in the 2 crewmembers of Gemini VII (48). Figure 4 is an illustration of the graded exercise test results of a Gemini IX crewmember (12). Although these were not true measurements of VO_2max, the investigators suggested that these data provide strong evidence that aerobic capacity was compromised following the Gemini flights. The pre- to postflight decline in oxygen consumption at test termination was suggested to have been related to decreased total blood volume (reduced in 5 of 6 crewmembers examined), plasma volume (decreased in 4 of 6) and red cell mass (decreased in all 6 crewmembers). The factors that were speculated to cause these hematological changes were hyperoxia (the Gemini space craft environment was 100% oxygen at 5 psia, or 259 mmHg), physical confinement of the crew, dietary factors, and weightlessness.

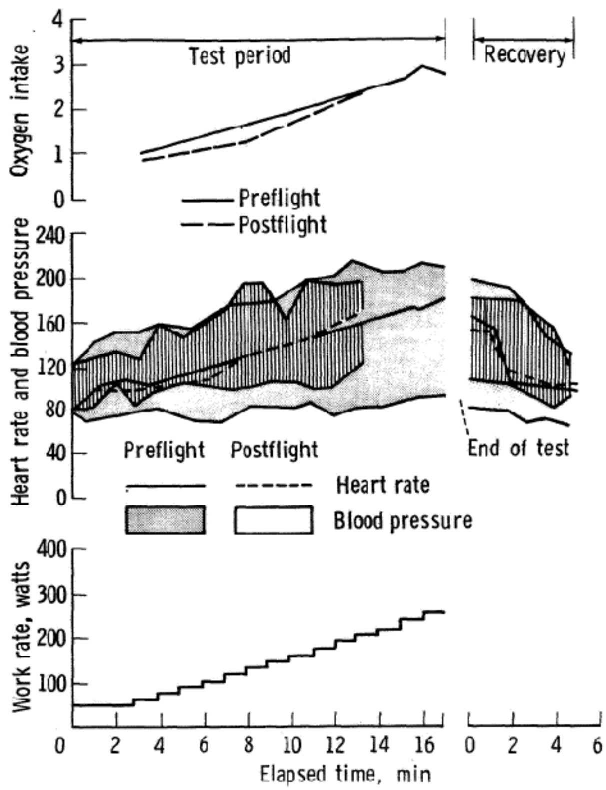

Figure 4. Gemini IX pre- and postflight exercise test results.(12)

3. Apollo Program

The Apollo program is best remembered for the flight of Apollo 11, which was the first manned exploration of the moon. The Apollo program consisted of 11 flights conducted between 1968 and 1972. Of these flights, six delivered astronauts to the moon's surface. The Apollo crews consisted of 3 men per flight and the flight durations ranged from 5.9 to 12.7 days.

The crews of Apollo 7-11 and 14-17 (n=27) participated in submaximal exercise testing to quantify pre- to post flight changes in the physiological response to exercise (11;143;144;146). An electronically-braked cycle ergometer was used for exercise testing with which work rate was controlled using a HR feed-back loop, and VO_2 (L/min) was measured during these exercise tests.. The test protocol consisted of 3 exercise work rates which produced HRs of 120, 140 and 160 beats·min^{-1}. The Apollo 9 and 10 crews also performed an additional stage which elicited a HR of 180 beats·min^{-1}. The oxygen consumption (that is, exercise work rate) at all exercise stages was significantly less on landing day (R+0), but was near pre-flight levels 24-26 hours following landing (R+1; **Figure 5**). Exercise Qc measurements also were obtained from the crews of Apollo 15-17 and indicated that a reduction in SV (from 145 ± 34 ml·beat^{-1} to 92 ± 34 ml·beat^{-1}) led to the increased HR response to exercise on R+0. Although the HR response to exercise increased, the increase was not enough to compensate for the decline in SV as Qc was 37% lower on R+0 than it was before flight; however, it was only 7% reduced (not statistically different) from preflight on R+1. The mean pre- to postflight change in plasma volume of the Apollo astronauts was -4.4 ± 1.7% on R+0 and +4.8 ± 2.2% on R+1 (98). The rapid normalization of the crewmembers' responses to exercise suggests that changes in plasma volume played a role in the postflight decline in VO_2 at the terminating workload.

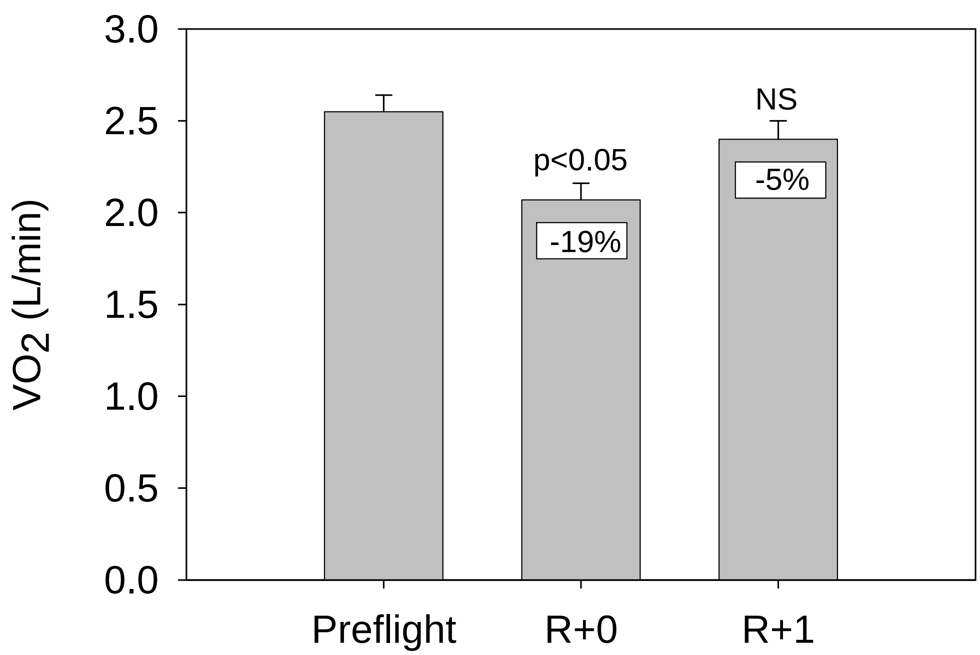

Figure 5. VO_2 changes at exercise stage eliciting a HR of 160 beats/min (Apollo crews n=27).

4. Skylab Program

The Skylab program was the first U.S. space station and the first experience with longer duration space flight. The station was launched in May 1973 atop a Saturn V vehicle, the last launch of the rocket that first took man to the Moon. Three crews traveled to Skylab using Apollo-era command modules launched on Saturn 1B vehicles. The missions were 28 days in duration (Skylab 2), 59 (Skylab 3) and 84 (Skylab 4). Medical activities accounted for approximately 7% of the mission time during flight.

During the Skylab missions, routine submaximal graded exercise testing was performed on a cycle ergometer, and expired metabolic gasses were analyzed to measure VO_2 (104;117) (**Figure 6**). The submaximal exercise test consisted of 5-minute stages of rest followed by exercise at work rates eliciting 25%, 50%, 75% and 25% of preflight VO_2max. Preflight VO_2max was established during previous graded exercise tests to volitional fatigue conducted at L-360 and repeated at L-180. The submaximal exercise test was repeated approximately every 6 days during each flight, starting with flight day 6. There was no trend in the in-flight submaximal HR data, which was taken as an indicator of no change in the aerobic fitness of the crews; the in-flight HR at the 75% work rate was not significantly changed from preflight values in 8 of the 9 crewmembers. Cardiac output was not measured during flight, but it was measured during the exercise tests performed before and several times following flight (50). The mean Q_c of all crewmembers at the 75% work stage was decreased by approximately 30% and SV was decreased by 50% on R+0. Within 10 days after landing, Qc and SV were within 10% of preflight values, but complete recovery was not noted until 31 days following flight. The HR response to exercise was markedly elevated immediately following flight and gradually returned to preflight levels by R+24 days. Plasma volume declined by 12.5% on R+0 and returned to preflight values by R+14 days (85). These changes did not appear to be related to mission duration. Although VO_2max was not measured in these subjects, the postflight exercise responses were assumed to be consistent with a decrease in aerobic capacity during the early recovery period and a gradual return to preflight levels over the month following flight.

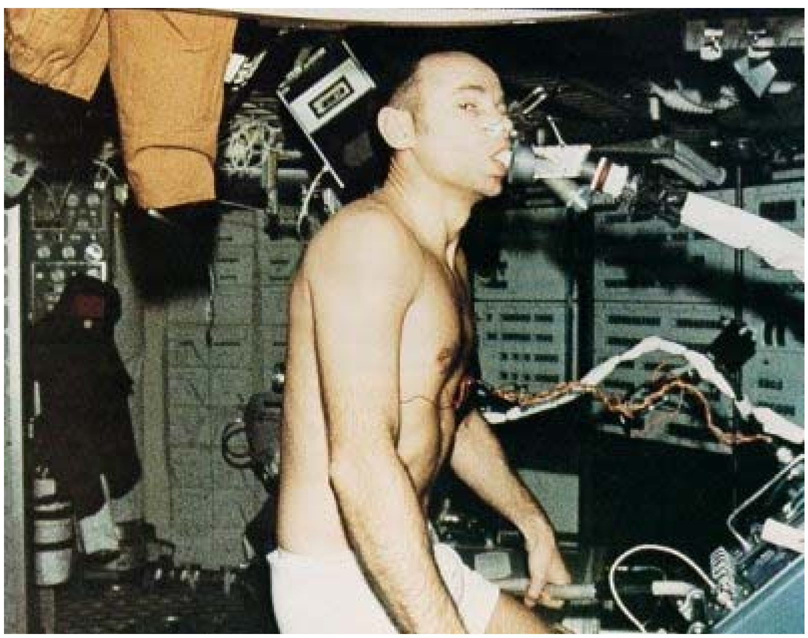

Figure 6. Skylab crewmember performing cycle exercise test with VO_2 measurements.

An attempt was made to collect VO_2max data during instrumented personal exercise sessions to near-maximum exercise levels on four crewmembers of the Skylab 3 and 4 missions (152). However, a number of problems prevented accurate measurement of VO_2max. The Skylab cycle ergometer was limited to a work rate of 286 Watts, and 3 of the 4 crewmembers were able to exceed this work rate during preflight testing. Therefore, these 3 crewmembers performed prolonged work at 286 Watts during flight to elicit a “maximum work load.” The limiting factor for these sessions was leg fatigue, rather than a true cardiovascular maximum effort. The device that measured expired ventilation (a component of the measurement of VO_2) could only accurately measure values up to 150 $L \cdot min^{-1}$, and this level was exceeded in several tests, possibly because of the low cabin pressure of Skylab (259 mmHg). The investigators concluded that the VO_2max of the crewmembers was likely maintained and perhaps even increased during flight, although the measurement hardware limitations greatly cloud the interpretation of the data.

5. Space Shuttle Program

The first launch of the Space Shuttle program was in April 1981. The Space Shuttle is unique in that it is the first winged space vehicle that is designed to be launched from the ground and return to Earth to be reused. There have been five Shuttle orbiters, two of which were destroyed – one during launch (*Challenger*, January 1986) and the other during deorbit operations (*Columbia*, January 2003). The payload capacity of the Space Shuttle is considerable (22,700 Kg mass and 1,106 m^3 volume). Five to seven astronauts typically fly on a Space Shuttle mission. The intended use of the Space Shuttle from its inception was to support a future space station, which at the time of this writing is the primary use of the vehicle. However, for the majority of the Space Shuttle program the vehicle has been used to transport large payloads into orbit (such as the Hubble space telescope) and to conduct other low-Earth operations. The Space Shuttle cargo bay was also used to carry a laboratory, such as the Spacelab and SPACEHAB™ modules, in which human life sciences experiments have been conducted.

The studies that have actually measured VO_2max prior to, during, and immediately following space flight have been conducted during the Space Shuttle era. Of these, only one study measured VO_2max during space flight. Levine et al. (111) reported the results of peak cycle ergometer tests on six astronauts during the Spacelab Life Sciences (SLS)-1 (9 day) and SLS-2 (14 day) missions. VO_2max measured between flight day 5 and 8 was not different than preflight VO_2max. Interestingly, submaximal Qc, measured on the same flights and same days as the astronauts reported on in the Levine study (111), was lower during space flight (161). Shykoff, et al. (161) speculated that either the Qc needed to support moderate to heavy exercise is less in microgravity than on the ground or that a reduction in circulating blood volume caused by the storage of blood in the pulmonary circulation limited the increase in Qc by reducing the SV. Reduced submaximal Qc during space flight is difficult to reconcile with the observation that VO_2max did not change during flight in these subjects (111). However, Alfrey and co-workers reported that plasma volume was reduced by 17% on flight day (FD) 1 and 12% on FDs 8-12 during these space flights (2). Subjects experienced a mean reduction in VO_2max and Qc of 22% and 24%, respectively, on landing day while there was no change observed in maximum HR. Levine and colleagues (111) concluded that the reduction in maximum Qc, and thereby VO_2max, was due entirely to changes in SV. The reduction in SV was likely due to impaired venous return caused by a decrease in plasma volume, which remained depressed on the first recovery day (2). VO_2max recovered by approximately 50% on R+1-2 and had fully recovered to preflight levels by R+6-9 (**Figure 7**). Plasma volume had recovered to preflight values on R+6 (2).

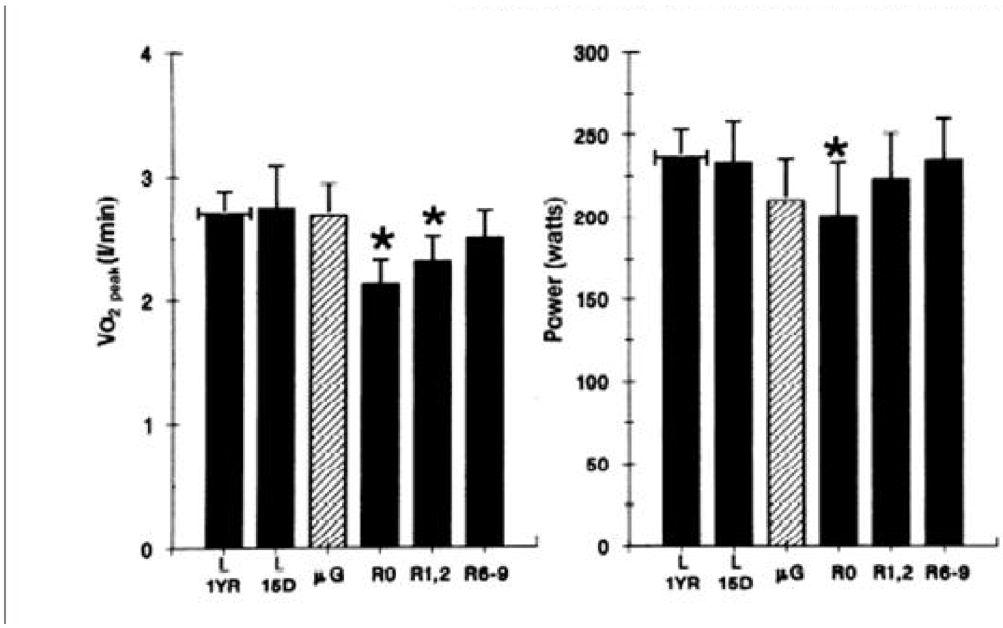

Figure 7. VO_2 max was not changed during the SLS-1 and SLS-2 flights; however it is decreased in the first 2 days following flight (111).

Moore et al. (121) reported exercise results that are consistent with the SLS-1 and SLS-2 findings. The primary intent of this study was to determine if maximal exercise performed on the last day of flight would preserve postflight orthostatic function and aerobic capacity, as suggested by a previous bed rest study by Convertino and coworkers (27). Astronauts (n=8) participating in flights ranging from 8-14 days in duration performed a peak cycle ergometer test before flight and again on the last full flight day. Although VO_2 was not measured during flight, the HR response to exercise during flight was not different from that measured preflight, and the peak work rate performed during these tests was not different than before flight. Both of these observations suggest that VO_2max was unchanged during flight. However, when VO_2 was measured during exercise testing on landing day, the crewmembers experienced a decline in VO_2max ranging from 11-28% (mean decline 18%). Three days following flight, VO_2max still was reduced an average of 11%, but VO_2max had returned to baseline values by R+14. Similar to the findings of Levine and colleagues (111), maximum HR did not change following flight; thus it is likely that the reductions in Qc and SV played a role in the decrease in VO_2max on R+0 and R+3.

In contrast to the studies reported by Levine et al. (111) and Moore et al. (121), Trappe et al. (178) reported results consistent with aerobic deconditioning during a Space Shuttle flight. Exercise tests were limited to 85% of preflight VO_2max during flight and up to 4 days following flight. The 4 subjects on the 16-day STS-78 flight demonstrated a mean increase of 7% in exercise HR at the 85% workload on FD 8 and 9% on FD 13, which was interpreted as a sign of aerobic deconditioning. The difference between these results and those reported previously (111;121) are not readily explainable, but may have been related to differences in the preflight fitness levels of the crewmembers participating in the studies (Trappe et al. (178): 3.59 $l \cdot min^{-1}$, Moore et al. (121): 3.29 $l \cdot min^{-1}$, Levine et al. (111): 2.76 $l \cdot min^{-1}$), exercise countermeasures and other physical testing performed during the flights, or individual differences in the response to space flight (degree of space motion sickness, medications used, etc.). It is also possible that, similar to the data observed by Shykoff et al. (161), submaximal Qc (caused primarily by a lower SV) was decreased in these subjects, and submaximal HRs were increased as a partially compensatory response. Cardiac output and SV were not measured in the study reported by Trappe et al. (178). On R+4 and R+8, VO_2max was reduced by 10.3% and 5.0%, respectively. This finding follows the general trend of recovery in VO_2max observed by both Levine et al. (111) and Moore et al. (121) .

Investigations related to exercise capacity and the preservation of the cardiovascular responses to exercise were conducted during the NASA Extended Duration Orbiter Medical Project (EDOMP) from 1989 to 1995. These studies were: 1) designed to be relevant to space flight operations, 2) required to be related to performance of the crewmembers during entry, landing, or egress from the Space Shuttle, and 3) conducted as NASA Detailed Supplemental Objectives (DSOs). DSO studies are limited in the amount of hardware stowage that can be used to support the studies during flight; therefore, the majority of these involved pre- vs. postflight comparisons. In addition, fairly early in EDOMP, NASA's Committee for the Protection of Human Subjects limited the intensity of exercise investigations during and immediately following space flight to levels of no greater than 85% of preflight VO_2max. The authors of this report are not aware of any cardiovascular anomaly that occurred either during or following flight that precipitated this exercise limitation. In any event, this restriction is the reason for the limitation of exercise intensity of the subjects of Trappe et al. (178) and for subsequent investigations. The study reported by Moore et al. (121) was the final investigation which utilized maximum exercise testing during or immediately following Space Shuttle flight.

Despite the above listed limitations, studies conducted during the EDOMP era produced findings related to the space flight-induced decrease in aerobic capacity. One study examined the effects of continuous vs. low-level interval exercise on postflight aerobic capacity (162). During flight the subjects (n=17) performed one of two exercise prescriptions on a small passive treadmill or served as controls (**Figure 8**). HR was used by the exercising crewmembers to regulate exercise intensity. Treadmill testing to measure VO_2max was performed before and 2 days following flight. The subjects who exercised during flight demonstrated no statistically significant decrease in VO_2max, while the control subjects experienced a 9.5% loss. Although this study did not measure VO_2max immediately following flight, it did demonstrate that VO_2max response 2 days following flight could be altered by in-flight training.

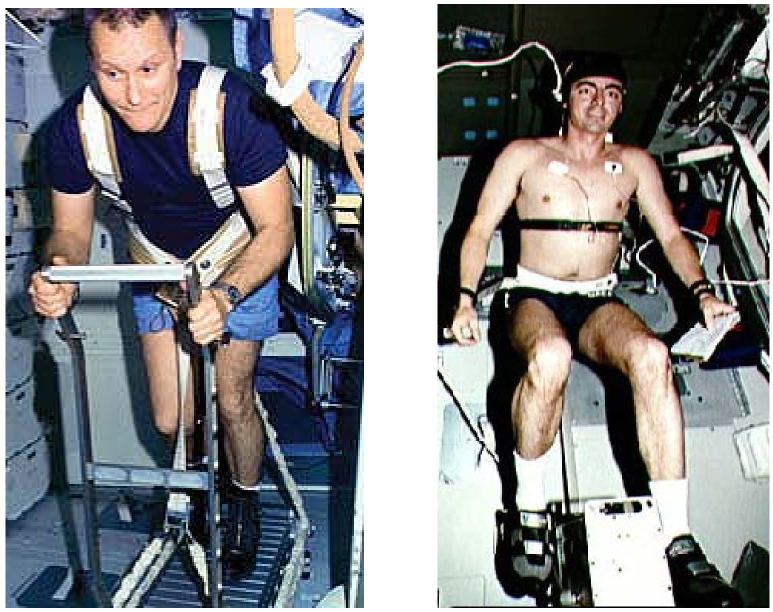

Figure 8. Astronauts exercising on passive space shuttle treadmill and the Shuttle cycle ergometer.

Another study conducted during EDOMP was designed to monitor aerobic exercise performed during flight and the influence of this exercise on the HR and VO_2 responses to exercise testing following flight (67). Astronauts (n=35) performed incremental (50 Watts for 3 minutes, followed by 50 Watt increases every 3 minutes) upright cycle ergometer exercise tests with VO_2 and HR measurements prior to flight (L-10) and on landing day (R+0). These tests were terminated at the work stage that elicited 85% of each participant's age-predicted maximum HR; VO_2max was not measured. Exercise countermeasures for use during flight were not prescribed, but each astronaut wore a HR monitor that recorded both the HR and duration of their exercise sessions. One mission included both a treadmill and a cycle ergometer as exercise modalities, but the treadmill was used for only two exercise sessions by one crewmember. The remaining inflight exercise conducted during this study was performed on the Space Shuttle cycle ergometer. The major finding of the study was that astronauts who performed regular aerobic exercise (defined as three or more sessions per week, each session lasting at least 20 minutes, and at an intensity that elicited a HR of > 70% of their age-predicted maximum HR) demonstrated a smaller decline in VO_2 at the termination workload (thus their exercise HR was less elevated) than did astronauts who exercised less frequently or at a lower intensity (**Figure 9**). Q_c was not measured in these subjects, but the relative tachycardia experienced by the crewmembers on landing day is consistent with a compensation for lowered SV. Though speculative, it is possible that plasma volume was better maintained in the "regular exercise" subjects. Lee et al. who reported on the R+0 stand test findings of these subjects (103), observed a greater HR response and reduced pulse pressure (often used as an index of SV) during standing in the "minimal" exercise subjects. Thus, it appears that, at least for Shuttle duration flights, a decline in VO_2max immediately following flight may be partially attenuated by exercise conducted during flight.

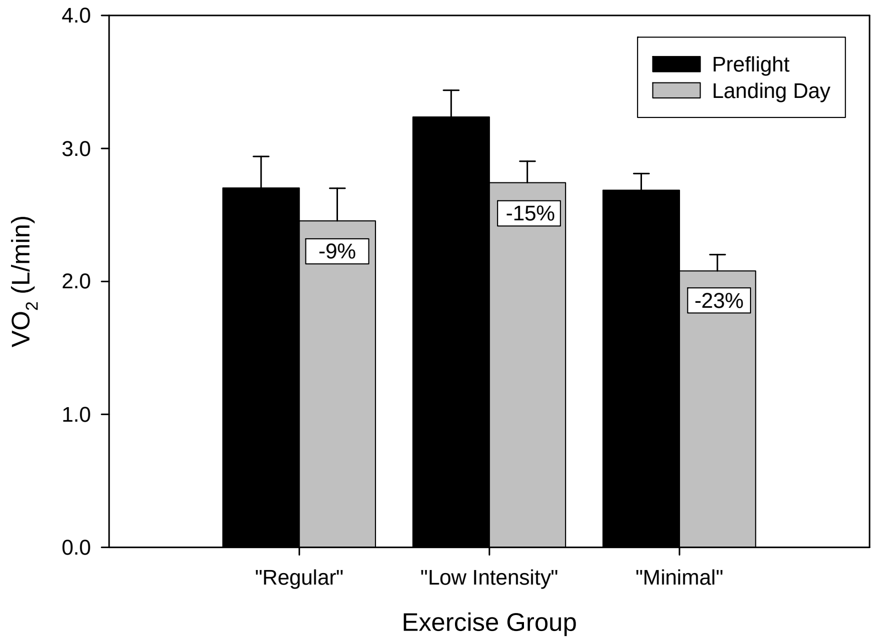

Figure 9. Oxygen consumption achieved at 85% age-predicted maximum HR pre- and post-flight in crewmembers (n=35) who participated in different amounts of in-flight exercise.
"Regular" (n=11) - Exercised > 3x/week, HR > 70% age-predicted, > 20 min/session
"Low Intensity" (n= 10) - Exercised > 3x/week, HR < 70% age-predicted, > 20 min/session
"Minimal" (n=14) - Exercised < 3x/week, HR and min/session variable (from Greenisen et al. (67)

6. International Space Station (ISS)

The ISS is an orbiting research facility that, at the time of this writing, is still being assembled in low-Earth orbit. ISS assembly in space was initiated in 1998, and a manned presence on board ISS has continued since November 2000. The crews of the ISS have been comprised of U.S., Russian, European Space Agency (ESA), and Japan Aerospace Exploration Agency (JAXA) astronauts, and the crew size for ISS Expeditions has varied between two and six long-duration occupants. Most major components of the ISS were launched on the Space Shuttle, except for the Zarya and Zvezda modules (launched on Russian Proton-K vehicles) and the Pirs docking compartment (launched on a Soyuz-U booster). Supplies and crewmembers are ferried to and from ISS on both the Space Shuttle and Russian vehicles.

A treadmill, two cycle ergometers, and two resistive exercise devices currently are available for use by ISS crewmembers to counter the effects of long-duration space flight exposure. However, equipment availability and crew member utilization has varied throughout the history of the ISS. The Russian crewmembers follow a set of exercise countermeasures prescribed by Russian specialists (92). Typically, the remaining crewmembers perform 4-6 treadmill exercise sessions sessions$\cdot$wk^{-1} for 30-45 minutes, 2-3 cycle ergometer exercise sessions$\cdot$wk^{-1} for 30-45 minutes, and up to 6 resistive exercise training sessions$\cdot$wk^{-1}. Although upper body exercises are possible, crewmembers primarily perform resistive exercise to maintain strength in the lower body and trunk. Two and one-half hours per day is scheduled for exercise sessions, including time to change into exercise clothing and clean up following activity, so the effective daily exercise time is approximately 1 hour and 30 minutes or less (104).

The treadmill (TVIS – Treadmill with Vibration Isolation System**, Figure 10)**) is similar to a standard treadmill, except that crewmembers must use a harness and loading system to keep them on the belt surface (115). Additionally, the TVIS is vibration isolated from ISS using a set of active counter masses and a large gyroscopic device that are located under the device. In most cases, the treadmill belt is driven by a motor, and the speed is adjustable from 0 to 10 miles$\cdot$hr^{-1} (0 - 16 km$\cdot$hr^{-1}) in 0.1 miles$\cdot$hr^{-1} (0.16 km$\cdot$hr^{-1}) increments. However, some crewmembers have chosen to use TVIS in the non-motorized mode in which they must drive the treadmill belt (107). The non-motorized mode also can be used in cases when the motor is not functioning. The TVIS was delivered for use on ISS during Expedition 2. Another treadmill, an enhanced second generation device, will be soon delivered support six crewmembers' daily exercise requirements.

Figure 10. International Space Station crew members exercising on the Treadmill with Vibration Isolation System (TVIS; left), the cycle ergometer Treadmill with Vibration Isolation System (CEVIS; center) and the Russian velo-ergometer (right).

Two cycle ergometers are available for use on ISS, one NASA-provided and one Russian-built. NASA's Cycle Ergometer with Vibration Isolation System (CEVIS), delivered to the ISS during Expedition 2, is an ergometer configured similar to a semi-recumbent cycle that is vibration isolated from the ISS using a counter mass system and a passive system of wire isolators located on the corners of the frame (130). The CEVIS is capable of exercise loads from 25-350 Watts in 1 Watt increments and allows stable work rates to be applied between pedaling rates of 50-120 rpm. The second cycle is a Russian-designed cycle ergometer known as the veloergometer. The veloergometer was delivered to ISS for Expedition 1 and is capable of controlled loads ranging from 100 to 250 Watts in 25 Watt increments. Unlike the CEVIS, the veloergometer is not vibration isolated.

Although it is not a device designed to support aerobic training, the interim Resistive Exercise Device (iRED, **Figure 11**) is used onboard ISS to aid in the maintenance of muscular strength (102;155). The iRED consists of two canisters, each containing a series of elastomer-spoked wheels known as "FlexPacks." A non-elastic cable attached to the stack of FlexPacks is routed through a spiral pulley and extends from the base of each canister to either a body-worn harness or an exercise bar. Extending the cables during the concentric portion of an exercise turns a splined shaft and rotates the inner-ring of the FlexPacks; this stretches the elastomer spokes and generates a resistive force. An eccentric load is generated as the cable subsequently recoils. Rotating a handle attached to the top of each canister alters the initial stretch of the FlexPacks and allows the user to adjust the magnitude of the resistive force.

Figure 11. International Space Station crewmembers exercising on the interim Resistive Exercise Device (iRED; left) and the Advanced Resistive Exercise Device (ARED; right).

There are several limitations of the iRED which likely have reduced its effectiveness (155). First, the combined maximum load of both iRED canisters is only 300 lb. (136 kg) of force. This is much lower than can be performed by most crew members during certain exercises, particularly the squat and heel raise exercises, because the crew members are not lifting their body weights. Second, the eccentric-to-concentric force ratio is only ~60-80% (102). Third, during early ISS missions iRED's function was unreliable, and the number of sets and repetitions that a crewmember was allowed to perform was limited to increase the life of the FlexPacks. Subsequently, the FlexPack material was redesigned and replaced in 2003 with a thicker elastic material and other more robust design features.

In the meantime, NASA engineers designed and built a new Advanced Resistive Exercise Device (ARED) with a maximum load of 600 lb. (272 kg) and a >90% eccentric-to-concentric ratio. The ARED was designed to simulate the loading of free weight exercises through the use of a pair of vacuum cylinders as the primary loading mechanism, which is enhanced to simulate the effects of inertia using flywheels (54). The ARED was delivered to the ISS during Expedition 18, and the first crewmembers to use the device returned very favorable comments (Col. E. Michael Fincke, personal communication).

Cycle ergometry has been used for exercise testing of U.S. and other international partners' crewmembers before, during and after ISS missions for medical monitoring purposes. Pre- and post-flight testing has been performed on an upright cycle ergometer at the NASA Johnson Space Center Exercise Physiology Laboratory in Houston (the preflight and late post-flight location) or at the Gagarin Cosmonaut Training Center in Star City, Russia (early post flight location for most tests after flight). Regardless of the testing location, the same model cycle ergometer (Excalibur Sport™, Lode BV, Groningen,Nederland) is used for testing. The initial pre-flight test, performed approximately 9 months before launch, is a test to maximal exertion to measure pre-flight VO_2max and maximal HR. Thereafter, submaximal exercise tests are performed because of restrictions on maximal exercise testing similar to those imposed during EDOMP. The submaximal test, which is known as the Periodic Fitness Evaluation (PFE), is a continuous protocol consisting of four five-minute stages at work rates equivalent to 25, 50, 75, and 25% of pre-flight VO_2max; this protocol is comparable to that used during the Skylab program (118). PFE testing is scheduled to be performed approximately 30 days prior to launch, flight day 15, every 30 flight days thereafter, and five and 30 days after landing. However, during flight, PFE tests are sometimes waived or rescheduled for days other than the planned test date due to mission-related events, such when a Space Shuttle is docked to ISS or during an EVA. In addition, if an EVA is scheduled to be performed in the Russian Orlan EVA suit, the crew members perform a Russian exercise test, designated as MO-5, instead of the PFE prior to the EVA and the PFE is typically waived for that month. The PFE exercise tests during flight are performed using the CEVIS.

The HR response to the standardized cycle ergometer work rates in the submaximal exercise tests have been interpreted as an index of aerobic conditioning and an extrapolation of the HR-VO_2 relationship has been used to estimate changes in VO_2max during and after flight **(Figure 12)**. Although the linear extrapolation method is commonly used during field testing of subjects (8), it has not been specifically validated during space flight. Further, this technique (5) is a good indicator of the mean VO_2max of a group, but the variation from true VO_2max in an individual can occur (110). The changes in estimated VO_2max, particularly those derived from testing during flight, should be viewed in light of these limitations.

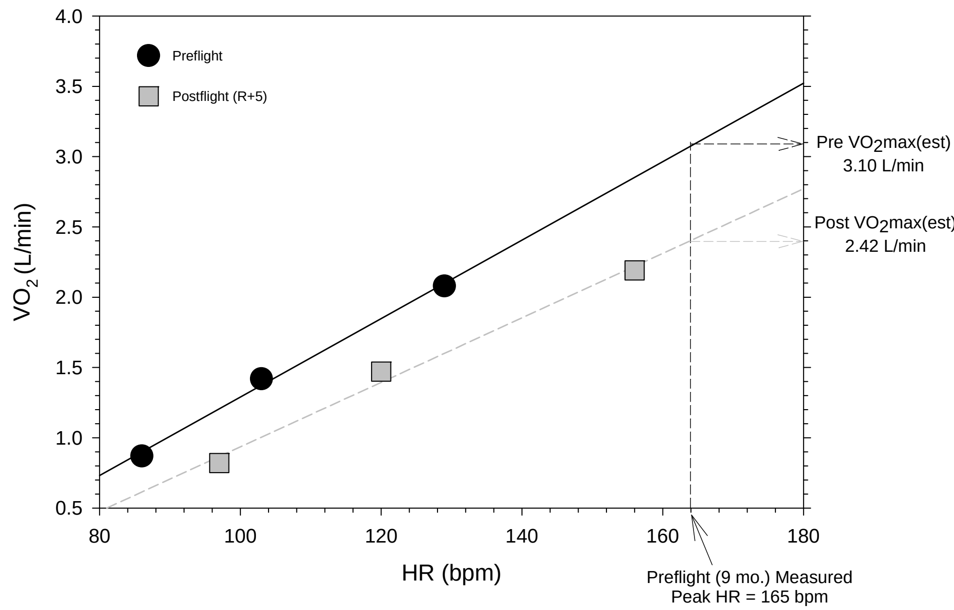

Figure 12. Example of linear extrapolation method of estimating VO_2max.

Results from the in-flight submaximal exercise tests of nine U.S. crew members who performed the PFE test at least once every 50 days during ISS flights lasting >150 days indicate that the HR response to exercise is elevated early in ISS missions (**Figure 13**). Using this information, VO_2max is estimated to decrease by 15% below pre-flight levels at the start of a mission (151). As the mission progresses the HR response to exercise, thus the estimated VO_2max, recovers by the end of a flight. This recovery is presumably due to the regular performance of exercise countermeasures.

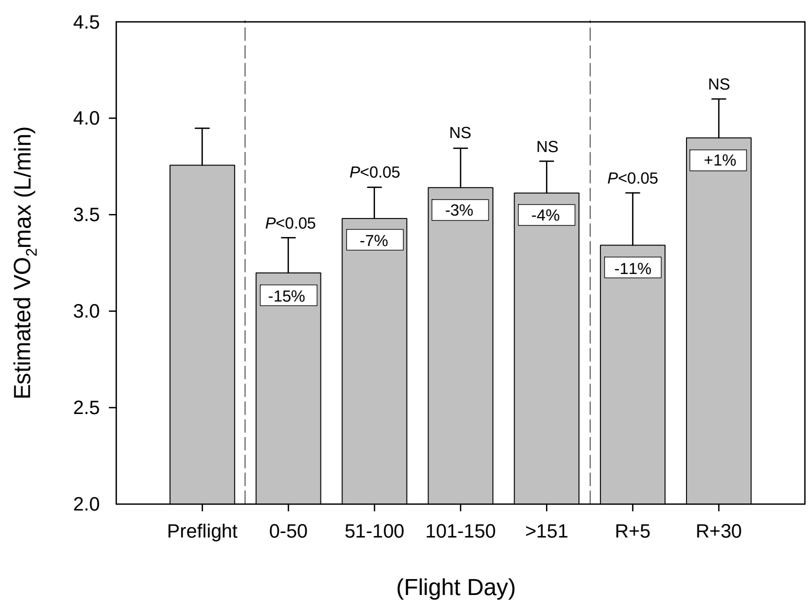

Figure 13. Percentage change in VO_2max during ISS flights, estimated from changes in the HR response during submaximal exercise tests.

These results from US crewmembers are remarkably similar to the MO-5 cardiovascular exercise test data from four Russians cosmonauts during ISS (137). Russian cosmonauts perform the MO-5 cycle test every 30 days during flight. The Russian test protocol consists of three-minute stages at 125, 150, and 175 Watts using the veloergometer. The HR response to exercise of these cosmonauts was greatest during the test that was performed one month into flight and progressively decreased as flight duration increased. The authors of the Russian report referred to the initial phase of flight as a "dead period" during which the decrease in physical condition is so severe that none of their countermeasure regimes were sufficiently effective. However, Russian crewmembers exercise little during the first two weeks during flight, which may contribute to the increased HR response noted early during flight.

Following missions to the ISS, VO_2 measured during the submaximal exercise test are not different than preflight, but the HR response to the same absolute exercise work rate is elevated on R+5. Plasma volume is normalized to preflight levels by R+5 (Dr. Steven Platts, personal communication), therefore the elevation in HR may be due to a combination lowered erythrocyte mass and muscular detraining. The ISS estimated VO_2max values decline an average of 16% from preflight values (**Figure 13**), which is similar to the actual VO_2max change on R+0 during Shuttle flights (111;121). This is much greater than that reported between R+1 and R+9 in Shuttle crewmembers (177), suggesting that the deconditioning experienced by ISS crew members is greater, or lasts for a longer duration than that experienced by Shuttle crews. The HR response to exercise is not different than pre-flight by R+30, and therefore it is assumed that VO_2max is recovered in ISS crew members by this time. It is unclear, however, if VO_2max had recovered to pre-flight values at an earlier time.

7. Limitations in the Interpretation of Long-Duration Aerobic Exercise Data from ISS

Interpretation of the inflight exercise HR data in US ISS crewmembers has been based upon the assumption that work rates on the CEVIS would produce similar metabolic rates as observed during pre-flight testing. Although the Skylab submaximal exercise VO_2 data support this assumption (118), it has not been possible to measure exercise VO_2 on board ISS until recently. Routine in-flight VO_2 measurements were originally planned during the PFE tests, but launch vehicle payload constraints, payload priorities, and budgetary issues prevented a metabolic gas analysis system from being flown to the ISS until Expedition 13. Preliminary data recently collected from seven ISS astronauts indicate that in-flight submaximal VO_2 differs from preflight values at the lowest and highest work rates during the PFE (Alan Moore et al., unpublished results). In the Skylab crewmembers, the inflight VO_2 may have been more consistent with preflight data because the Skylab cycle was hard-mounted to the vehicle floor. In contrast, the vibration and isolation system of CEVIS allows the cycle to sway during exercise. It is likely that a portion of the mechanical work expended by the crewmember is used to counter movements of the CEVIS which decreases cycling efficiency.

Using the VO_2 and HR data measured from the seven ISS crewmembers, we have extrapolated the PFE exercise data to estimate VO_2max, rather than estimating VO_2 based upon CEVIS work rate (Alan Moore et al., unpublished results). Our preliminary analyses indicate that the decrease in estimated VO_2max is not as extreme as first believed and further suggests that VO_2max may be maintained during flight with the current level of exercise countermeasure performance.

Given the uncertainty that exists regarding changes in VO_2max during long duration flight, we began obtaining measured VO_2max in an ISS experiment that began in late 2009. Crewmembers perform the standard PFE test protocol to 75% of pre-flight VO_2max. After completing this exercise stage, the work rate is incrementally increased 25 W each minute until the crewmember reaches maximal effort. Concerns with respect to maximal exercise during space flight have diminished recently with the addition of an automated external defibrillator on ISS, enhanced crew medical screening for crewmembers, and a history of multiple long duration flights with no reported significant cardiac dysrhythmias.

8. Flight Data Summary

As early as the Gemini Project, data exists – although limited – suggesting that during short-duration space flight the HR response to exercise, and likely VO_2max, is well-maintained but the postflight response is significantly compromised. The flight data of Levine (111) is the only conclusive evidence that VO_2max is unchanged during short-duration space flight, and the maintenance of work capacity during flight as reported by Moore (121) is strong corroborating data. However, contradictory data also exists (178) and may be partially explained by differences in the initial aerobic capacities of the crews and other factors unique to the subjects and missions.

There have been no direct measurements of VO_2max either during or immediately following long-duration space flight. Measurements of HR response to submaximal exercise during long-duration space flight have yielded conflicting results. The data from Skylab, showing no elevation in exercise HR response to exercise during flight, would seem to indicate that aerobic capacity is not altered during flights of up to 84 days (145). However, the data collected on board ISS by both the U.S. and Russian scientists and crewmembers show an elevation in the HR response to exercise that is pronounced early in flight (<45 days) and slowly returns toward preflight values (120;137). This seems to indicate that aerobic detraining occurs rapidly during flight. With the performance of inflight exercise countermeasures, however, the degree of detraining may be attenuated and reversed. Interpretation of the ISS in-flight findings must be viewed with caution as preliminary data also suggests that the oxygen cost of performing submaximal cycle exercise may be altered in ISS, perhaps due to factors related to the vibration isolation of the CEVIS.

There have only been two studies that have measured VO_2max upon landing and both of these studies were conducted following short-duration missions. The data consistently demonstrate that VO_2max is lower on landing day than it is before flight and that VO_2max recovers within 6-9 days after landing (111;121). Data from submaximal exercise tests conducted in the Gemini (12), Apollo (144), and Shuttle (7;67;177) programs all support the notion of reduced aerobic capacity immediately following flight with a rapid recovery. Data collected after long-duration space flight is confined to measurements conducted during submaximal exercise tests. Nevertheless, these data appear to be consistent with aerobic deconditioning in the first week following flight, with a return to baseline measurements within a month (120;137).

9. Effect of Reduced VO_2max on Space Flight Operations

The goal of any countermeasure to space flight exposure is to preserve the capability of the crewmembers to perform daily tasks and maintain a reserve to enable survival in emergency situations. With regard to routine tasks conducted on board the ISS, the preservation of aerobic capacity is not likely important as there are few, if any, physically strenuous routine tasks that are performed. EVAs typically elicit an average metabolic cost of ~ 200 $kcal \cdot hr^{-1}$(~0.7 Liters $O_2 \cdot min^{-1}$) and have ranged up to 500 $kcal \cdot hr^{-1}$ (~1.7 Liters $O_2 \cdot min^{-1}$) (71). The upper value represents approximately 50% of the typical astronauts aerobic capacity; however, because EVA activity is predominantly upper body in nature, and upper body VO_2max is approximately 70% of that measured in the legs, EVAs can become aerobically challenging. The metabolic cost of performing an emergency egress task in the NASA Launch and Entry suit has been reported as ranging from 2.0-2.7 Liters $O_2 \cdot min^{-1}$, depending upon the amount of G-suit pressurization employed (15). With regard to EVA on the lunar surface during the Apollo era, several EVAs reportedly were slowed by request of the medical personnel as heart rates during the activities reached 150-160 $beats \bullet min^{-1}$ (138). Until the mission scenarios are defined for future EVA work it is difficult to predict precisely what aerobic capacity will be required to successfully complete all tasks; however, it is likely that with extended stays on the moon or Mars, the importance of maintaining aerobic capacity will not diminish.

B. Ground-based Space Flight Analog (Bed Rest)

Justification: Human physiology studies during space flight are difficult to perform due to the limited number of subjects available and multiple confounding factors, including variable adherence to prescribed countermeasures, inconsistent dietary practices (163), participation in other science experiments, and interference of specific mission task requirements (178). Bed rest has become an accepted and established model to study changes in physiologic function associated with space flight, including changes in aerobic capacity (63), in a more controlled environment (134). In general, the reduction in VO_2max as a result of bed rest is considered to result from the combined effects of reduced physical activity and removal of the effects of orthostatic stress (26). In a direct comparison between responses after space flight and bed rest, Trappe et al. (178) reported that the decrease in aerobic capacity during supine cycle ergometry in 4 crewmembers 4 days after a 17-day mission (-10.4%) was comparable to that observed in 8 subjects (-6.6%) 3 days after a 6° head-down tilt bed rest of the same duration (Figure 15). No similar comparisons are yet available for long-duration missions and no bed rest studies have been conducted to mimic the countermeasure protocols in which astronauts and cosmonauts aboard ISS currently engage (76;92;93).

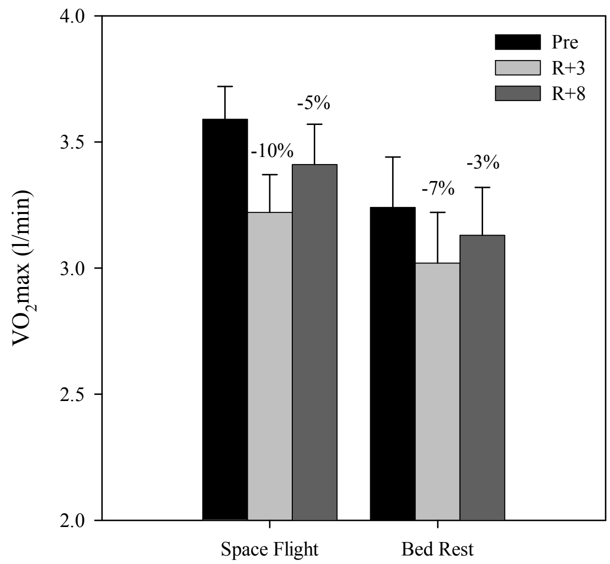

Figure 15. VO_2max before, 3 days after (R+3), and 8 days after (R+8) 17 days in space or bed rest (from Trappe et al. (178).

C. Changes in VO_2max with Bed Rest

1. Duration

In general, there is a rapid decline in VO_2max with the first few days of bed rest with a more gradual loss thereafter (26;31). Nixon et al. (128) reported a decrease in VO_2max, estimated from upright cycle ergometer test duration, of 22% (Pre: 36.4±2.4; Post: 28.5±2.0 $ml \cdot kg^{-1} \cdot min^{-1}$) following only 24 h of 5° head-down tilt bed rest. During bed rest periods up to 30 days, the average decrease in aerobic capacity occurs at a rate of 0.8-0.9 $\% \cdot d^{-1}$ (28;31;33). However, if aerobic capacity continued to decrease linearly in this fashion, the decrease in VO_2max would be predicted to be 42% by 60 days and 72% by 90 days of bed rest, which overestimates the reduction in VO_2max in longer duration bed rest studies, and would reach zero (death) within 122 days (23).

Capelli et al. (23) proposed an alternative model based upon measurements during 14, 42, and 90-day bed rest studies. Subjects in their studies experienced a decrease in aerobic capacity of 14% on day 14, 16% on day 42, and 32% on day 90 of bed rest. These investigators suggested that most of the decrease in exercise capacity occurs in the first 2 weeks and that the rate of decline is much smaller thereafter. The authors speculated that the initial rapid reduction in aerobic capacity was due to decreased maximal Qc and circulating hemoglobin levels, while the later slow progressive component was related to muscle atrophy and impairment in peripheral gas exchange. Similarly, Greenleaf et al. (69) observed the greatest rate of decrease in VO_2max in the first week of bed rest.

Decreased aerobic capacity (30) and delayed oxygen kinetics (39) during the first one to two weeks of bed rest generally are associated with decreased circulating blood volume. However, with longer simulated microgravity exposures, structural changes in the myocardium (49;135) and the vasculature (195) may increasingly impair exercise capacity as the duration of bed rest increases. Perhonen et al. (135) suggested that cardiac compliance and filling are reduced as the bed rest duration increases beyond 2 weeks. Additionally, negative metabolic adaptations to simulated microgravity, such as reduced citrate synthase activity in skeletal muscle, become apparent after 4 weeks of unloading (10;81). Longer durations of bed rest are associated with decreased muscle mass, strength, and endurance which would be expected to impair aerobic exercise performance and decrease the efficacy of the muscle pump to protect venous return (193).

2. Pre-Bed Rest Fitness

Taylor et al. (176) and Saltin et al. (148) were the first to report that men with a higher aerobic capacity had a greater absolute reduction in VO_2max after bed rest than those with lower fitness. Several subsequent studies confirmed this hypothesis (40;44), but this has not consistently been the case (73). Greenleaf and Kozlowski (73) observed that this relationship was strongest when subjects performed a cycle ergometer test protocol, particularly when supine. Although they reported that the relationship was not strong during upright treadmill testing, recent data from a set of bed rest studies with twins in which subjects performed treadmill exercise tests after 30 days of bed rest did find a significant correlation between pre-bed rest fitness and the amount of loss in VO_2max in both male and female control (nonexercising) subjects (104;105;194). However, with respect to gender, Convertino et al. (40) reported that there was a significant relationship between initial VO_2max and VO_2max measured after 10 days of bed rest in middle-aged (r=-0.84) and young men (r=-0.78), but not in either middle-aged (r=-0.25, NS) or young women (r=-0.38). The lack of relationship between pre-bed rest VO_2max and the bed rest-induced loss in women in these earlier studies might be a consequence of the lower pre-bed rest VO_2max values measured in many of these subjects and the shorter bed rest duration.

3. Gender

Few studies have examined the effect of gender on the change in aerobic capacity after bed rest. Those that have been conducted consistently reported that although the male subjects had higher pre-bed rest VO_2max values than their female counterparts, the loss of aerobic capacity expressed as a percentage of the pre-bed rest values was independent of gender in bed rest durations up to 30 days (**Figure 16**) (31;40;44;86;104;105). However, the absolute decrease in aerobic capacity ($l \cdot min^{-1}$ or $ml \cdot kg^{-1} \cdot min^{-1}$) generally is higher in males than in the female subjects.

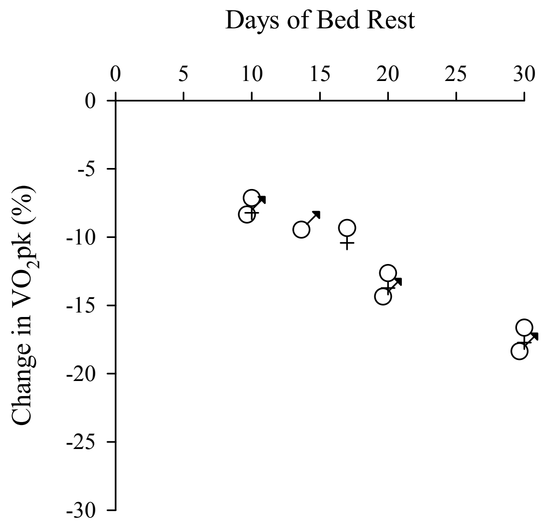

Figure 16. The percent change in aerobic capacity (VO_2pk) after bed rest is not different between men and women (104;105).

4. Recovery after Bed Rest

The time course of the recovery of VO_2max following bed rest is dependent upon the recovery of the physiologic variables that contribute to maximal exercise performance. Some improvement in exercise responses is apparent within a few days of reambulation. This is largely associated with a recovery of plasma volume, which is particularly apparent during submaximal exercise. For example, the HR response to treadmill walking was significantly elevated on the first day of reambulation following a recent 60-day bed rest study but was not different than pre-bed rest 2 days later, even though VO_2max was still significantly lower (-21%) than the pre-bed rest value (156). Although the specific recovery of post-bed rest plasma volume has not been well characterized, preliminary data from 90-day bed rest studies suggest that plasma volume on average is restored after 3 to 4 days of ambulatory recovery in non-exercise control subjects (Dr. Steven Platts, personal communication). There also appeared to be some recovery of submaximal HR, albeit less dramatic, during supine ergometry (150 W) 3 days after a 17-day bed rest period compared to the last in-bed rest test even though VO_2max was still depressed compared to pre-bed rest (-7%) (178).

Recovery of VO_2max normally occurs within 2 to 4weeks after bed rest (47), although for short bed rest durations the recovery process is well underway within one week. There was no significant difference from pre-bed rest VO_2max by 1 week following a 17-day bed rest study (-3.3%) (178), which was half the loss measured after only 3 days of reambulation (-6.6%). A similar amount of recovery (50%) was observed in four crewmembers after a space flight of the same duration (R+8: -5.2%, R+3: -10.4%). Subjects who experience longer periods of bed rest deconditioning may require more time to reach their pre-bed rest fitness levels. Saltin et al. (148) reported that the aerobic capacity of 3 of 5 bed rest subjects who participated in 21 days of bed rest was restored within 10 to 14 days after resuming normal activities. Additionally, more fit subjects appear to return to their pre-bed rest fitness levels more slowly than their less fit counterparts (148), although the previously more highly fit subjects are likely to perform better at all time points than if they had been previously unfit.

Following 60-day and 90-day bed rest studies conducted by NASA Johnson Space Center, VO_2max estimated from submaximal exercise tests was improved during the recovery period (from R+2 to R+11) in most subjects (Stuart Lee, unpublished results). However, VO_2max on BR+11 was still more than 10% lower than pre-bed rest VO_2max in 5 of the 9 subjects. All of the bed rest subjects participated in a daily 1-hour program of supervised ambulation and exercise during the post-bed rest period. The program consisted of 10-15 minutes of walking as well as calisthenics to strengthen the muscles of the trunk, upper body, and legs. The primary objective of the reconditioning plan was to restore the functional mobility and capacity to perform activities of daily living in preparation for release from bed rest. Since the protocol was not targeted specifically at increasing aerobic capacity, it is not surprising that recovery of VO_2max was incomplete. Similarly, Sundblad et al. (173) and Spaak et al. (33) observed that submaximal HR still was elevated 12 and 15 days, respectively, after a 42-day bed rest, but returned to pre-bed rest levels when tested again 32 days after the end of bed rest (173). In a separate study, VO_2max of supine subjects was restored during the 3 weeks of ambulatory recovery when subjects performed upright cycle ergometry for 1 hour per day at 50% of VO_2max for 10 days in the last week of recovery (169).

D. Mechanisms of Decreased Aerobic Capacity

In ambulatory subjects, it has been postulated that the primary determinant of VO_2max is maximal Qc (142). Although the debate continues in scientific journals to this day (129;149), many have argued that the capacity of the muscular system to increase vascular conductance and oxygen consumption is greater than the ability of the human heart to pump blood (6;147). Supporting the view that maximal Qc is a primary limiting factor after bed rest, the reduction in Qc in 5 male subjects following 21 days of bed rest (-26%) was similar to the reduction in aerobic capacity (-26%) (148). Similarly, using radionuclide imaging in 12 middle-aged men, Hung et al. (83) observed a 23% decrease in maximal Qc following a 10-day bed rest, which was similar to the decrease in VO_2max (17%). However, this relationship between the decrease in maximal Qc and lower VO_2max after bed rest does not appear to remain as the duration of the bed rest is extended. Capelli et al. (23) reported that decrease in Qc after 42 and 90 days of bed rest was not significantly different than that measured after 14 days of bed rest, suggesting that peripheral factors at the level of the working muscle were responsible for further decrements in VO_2max. In contrast, Ferretti et al. (57) reported that maximal Qc (-31%) was reduced to a greater extent than VO_2max (-17%).

1. Maximal HR

In general, maximal HR has been observed to be unchanged or increase slightly after bed rest (28;63), and therefore is not a contributing factor to a lower maximal Qc. Maximal HR was unchanged following 24 hours of bed rest (128), but in a separate study was observed to increase during both supine (5.7%) and upright (5.9%) cycle exercise following a 10-day bed rest (26). Convertino (30) suggested that during these bed rest studies there was a strong inverse relationship between changes in plasma volume and changes in maximal HR, but this has not consistently been the case. In separate investigations, maximal HR was not changed after 14, 42, and 90 days of bed rest (23). Maximal HR after bed rest does not appear to be influenced by the performance of an exercise countermeasure (169), but such results have not proven to be consistent. Recently, maximal HR was unchanged in control subjects following 30 days of bed rest, but was decreased slightly, but significantly, when an exercise countermeasure was employed (104).

2. Stroke Volume

The primary contributor to the decrease in maximal Qc, therefore, is a reduced SV. Hung et al. (83) reported that after 10 days of bed rest the reduction in Qc was solely the result of a 28% reduction in exercise SV. Similarly, maximal oxygen pulse, considered to be an index of SV, was reduced after 10 (27) and 17 days (178) of bed rest during supine ergometry, and comparable responses were noted in four astronauts following a space flight of the same duration (**Figure 17**) (178). Ferretti et al. (58) reported that the 31% decrease in maximal Qc following 42 days of bed rest was due solely to a 31% reduction in maximal stroke volume because maximal HR was unchanged. Resting and submaximal exercise SV also were reduced during long-duration bed rest (58;173;193) and space flight (9).

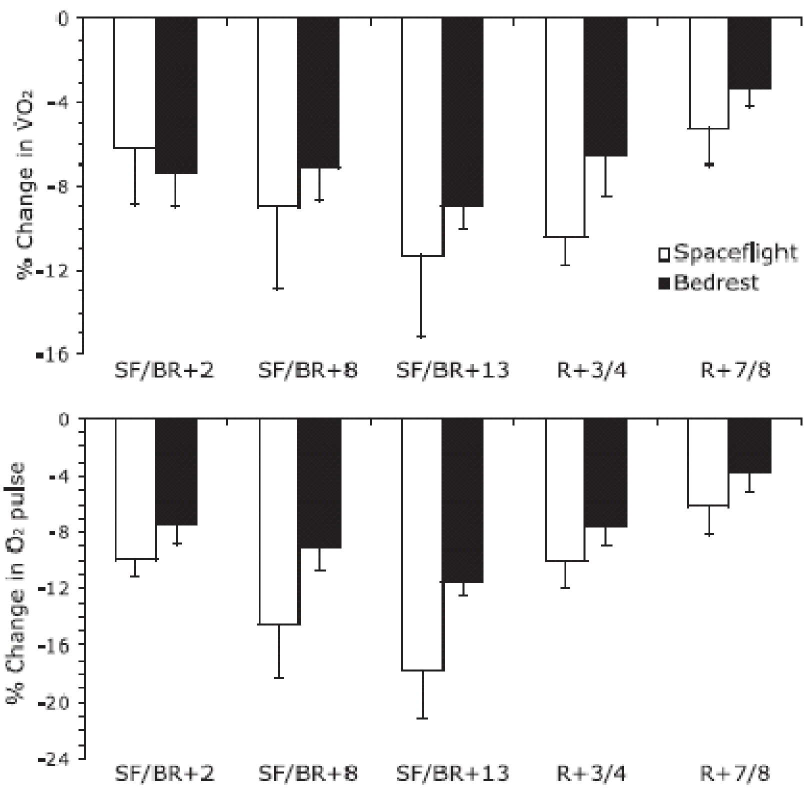

Figure 17. Oxygen consumption (VO_2) and O_2 pulse changes during exercise during and after both space flight and bed rest. Space flight data were collected at 85% of the pre-flight maximal workload, while bed rest data were collected at maximal effort (from Trapp et al. (178).

Although exercise SV is reduced with bed rest, ejection fraction is increased, suggesting that ventricular performance is maintained while venous return and cardiac filling may be impaired (31). Cardiac atrophy, measured using magnetic resonance imaging, appears to occur by 14 days of bed rest, which likely contributes to reduced cardiac distensibility and smaller SV for a given filling pressure. Left ventricular mass decreased in men by 5, 8, and 16% after 2, 6, and 12 weeks of bed rest, respectively (135). Additionally, left ventricular end-diastolic volume decreased by 14% after 2 weeks of bed rest but changed only minimally thereafter. Similar observations were made in women after 60 days of head-down tilt (49).

3. Venous Return

Decreased venous return may be the result of an increase in lower body venous compliance and reduced plasma volume that has been commonly observed after bed rest (31). Although multiple vascular factors contribute to limb compliance, changes in muscle mass and tonicity associated with bed rest may contribute to increased venous pooling when the mechanical obstruction to venous stretching and accumulation of blood is reduced. Following 30 days of bed rest, calf compliance was increased (2.4%) concomitant with a decrease in muscle volume (-5%) (35). In this bed rest study, changes in muscle cross-sectional area explained approximately 50% of the variability in the change in calf compliance. When subjects are exercising, it is recognized that cardiac filling pressure, SV, and Qc are supported by the expulsion of blood from the active muscles by the “muscle pump,” but these mechanisms will be of little importance in non-active muscles and other compliant regions of the circulation.

Blood may pool in other areas of the body after bed rest, including the splanchnic region, which would affect venous return during exercise. Savilov et al. (150) used radioisotope tracers to measure translocation of blood during LBNP, an orthostatic stressor. Subjects with low orthostatic tolerance displayed a marked increase in blood pooling in the abdomen during LBNP, with reflective decreases in blood distribution to the head and chest. Subjects with relatively better LBNP tolerance had less extreme responses. Similarly, Fischer et al. (59) reported that splanchnic blood flow was higher at each level of LBNP following just 4 hours of bed rest, and this was associated with an increased HR and reduced SV.

The reduction in vasoconstrictive reserve that Convertino and Cooke (34) suggest as a factor in orthostatic intolerance after bed rest and space flight also may contribute to reduced exercise capacity. Following 16 days of bed rest, elevated vasoconstriction was evident at rest in response to reduced plasma and SVs (53), and maximal vascular resistance was unchanged but was achieved at a lower level of orthostatic stress induced by a graded lower body negative pressure protocol (32). An inability to vasoconstrict – particularly in the venous system, which contains 70% of the total blood volume of a resting subject – impairs the ability to compensate for decreased blood and plasma volume, especially when coupled with orthostatic stress, to maintain venous return and SV during exercise.

Linked to this, changes in sympathetic nervous system response to exercise may be important to maximal exercise capacity with regard to the appropriate distribution of blood flow. Specifically, there is an inverse relationship between norepinephrine concentrations and splanchnic blood flow. Rowell (142) calculated, for example, that regional vasoconstriction in the splanchnic organs, kidneys, and skin can provide an additional 600 ml of O_2 per minute at maximal exercise in normal ambulatory subjects. Elevated levels of circulating norepinephrine may be an important adaptation to reduced blood volume to defend muscle blood flow and restrict flow to the splanchnic region and other inactive tissues (51). Sympathetic nervous system activity and catecholamine levels in resting subjects have been reported to be either unchanged or decreased following bed rest, and elevated HR in resting subjects has been ascribed to reduced vagal control (31). Following 3 days of bed rest, the norepinephrine levels during submaximal exercise tended to be higher and the norepinephrine threshold was lower in endurance athletes following bed rest, but these alterations were not evident in sedentary subjects (166). There was, however, no difference in maximal norepinephrine concentrations or epinephrine responses in either group. In contrast, following 16 days of bed rest, Engelke and Convertino (51) reported that plasma norepinephrine concentrations were 64% greater at peak exercise although peak HR was only 5% higher. However, no changes in epinephrine were reported during rest or maximal exercise.

4. Plasma Volume

Previous investigations consistently have demonstrated that plasma volume is rapidly reduced during exposure to space flight and bed rest, with the majority of the initial loss occurring within 1-2 days (17). Plasma volume has been observed to be decreased in as little as 6 hours, reaching a 10% loss in 24 hours (128), and equaling approximately 12% by the third day of bed rest. Greenleaf et al. (70) have suggested that the loss of plasma volume is progressive through 60 to 80 days of bed rest. The time course of the decrease in plasma volume is similar to the decrease in exercise capacity (**Figure 18**), and the mean loss of plasma volume across studies has been reported to account for approximately 70% of the variability in the mean decrease in VO_2max following up to 30 days of bed rest (31). Reduced circulating plasma volume may negatively affect exercise SV, the delivery of oxygen and nutrients to working muscle, and the removal of metabolic waste products. Thus, preservation of plasma volume has been suggested to be an important factor in the maintenance of exercise capacity during bed rest, and may be even more important during upright than supine exercise because of the addition of gravitational stress.

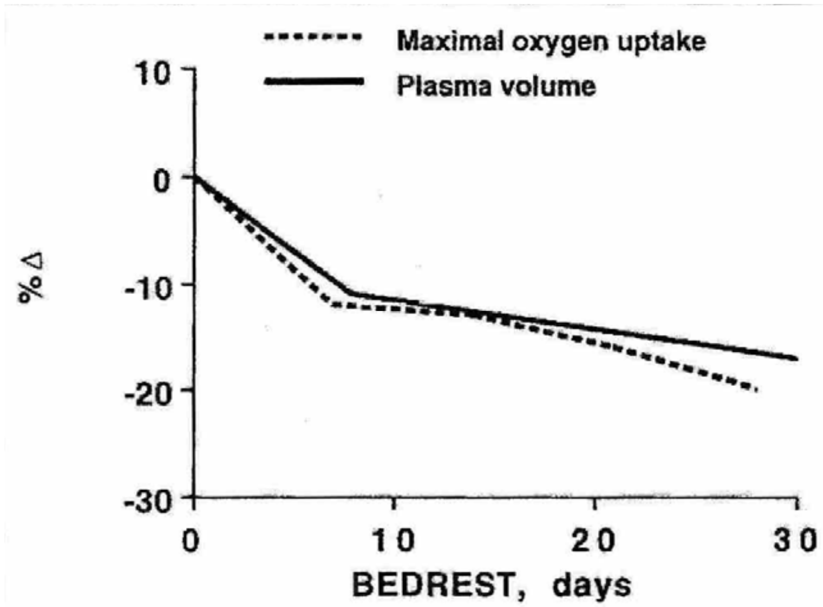

Figure 18. Decreased maximal oxygen consumption in subjects who perform no countermeasures appears to parallel losses of plasma volume up to 30 days of bed rest (31).

Maintenance of plasma volume alone is likely not the only determinant of exercise capacity preservation, especially following longer duration bed rest studies. Blomqvist et al. (18) provided sufficient amounts of saline through infusion to restore the central venous pressure to the pre-bed rest levels following a 24-hour bed rest. Although this procedure was not protective of orthostatic tolerance, it did abolish the loss of upright exercise capacity. However, Stremel et al. (169) maintained plasma volume (-8%, NS) in subjects during 14 days of bed rest by employing two daily 30-minute bouts of supine cycle exercise at 68% of pre-bed rest VO_2max, but supine VO_2max (-9%) and submaximal exercise responses were not maintained. In addition, subjects who performed an isometric exercise regimen during the same study experienced loss of plasma volume that was similar to the non-exercise control subjects (-15% vs. -10%), but the decrease in aerobic capacity was not as great (-5%) in the isometric exercise group. In a separate study, restoration of plasma volume at the end of a 16-day bed rest following an intense exercise bout did not successfully maintain aerobic capacity (52).

When reporting the results of plasma volume and maximal exercise capacity for individual subjects, the relationship between these two outcomes may not be as strong as when comparing mean results for a group of subjects. In general, there appears to be more variability in the plasma volume response to bed rest than in the decrease in VO_2max. Additionally, as the duration of the bed rest period increases, the strength of the relationship appears to decrease. Following 14 days of bed rest, in control subjects and subjects participating in a countermeasure employing a reverse pressure gradient garment, the decrease in VO_2max was significantly related to the loss of plasma volume (r^2=0.56) (43). Recently, in a study of male control and exercise countermeasure subjects, the change in plasma volume from pre-bed rest accounted for only 24% of the variance in upright exercise capacity after 30 days of bed rest (104). In a companion study utilizing female control and exercise subjects, there was no significant change in plasma volume in either the control or countermeasure subjects although the control subjects experienced a significant loss of aerobic capacity while the countermeasure subjects did not. The lack of change in plasma volume in both the female control and exercise subjects appears to support previous observation that exercise capacity is not strongly related to the change in plasma volume with bed rest (156).

5. Arteriovenous Oxygen Difference

Maximal systemic oxygen extraction, assumed to be at the level of the working muscle, does not appear to be affected by short-duration bed rest. There was little change in arteriovenous difference in middle-aged men following 10 days of bed rest (83), and it was unchanged after 21 days of bed rest in five male subjects (148). In general, the maximal extraction of oxygen from the systemic circulation does not appear to be specifically affected by bed rest, but oxygen extraction during submaximal exercise appears to be increased to compensate for the lower hemoglobin concentration during longer durations of bed rest (53). However, it is not clear from these data whether blood flow is appropriately directed to working muscle and whether the extraction at the level of muscle itself is maintained.

Delivery of oxygen to the muscle has been suggested to be impaired after bed rest. Resting leg blood flow (16) and peak vascular conductance (36;52), which has been associated with VO_2 max in ambulatory subjects (91;113;139;167), are reduced following bed rest. The reduction in vascular conductance was associated with a decreased resistance to fatigue of the calf muscle, but when peak vascular conductance was restored with a maximal bout of exercise at the end of bed rest VO_2max was not similarly protected (52). However, peak vascular conductance was associated with VO_2max before and after bed rest, suggesting that protection of peripheral mechanisms associated with the oxygen utilization in the muscle are not effective unless central cardiac effects are restored (52). Additionally, Hikida et al. (81) reported a 37% decrease in the capillary-to-fiber ratio of the soleus following 30 days of bed rest, although Ferretti et al. (56) observed no change in either capillary density or capillary-fiber ratio in the vastus lateralis.

6. Decreased Red Blood Cell Mass

Red cell mass has been reported to be decreased in as little as 7 days of bed rest (38), although most consistent results are observed at bed rest day 14 (63), and red cell mass may continue to decline for a short period during the recovery from bed rest (63;106;158). Convertino et al. (43) reported that red cell volume was decreased by 11% during 14 days of bed rest, independent of whether the subject performed no countermeasures or participated in a protocol to simulate the effects of orthostatic stress. Exercise during bed rest may prevent the loss of red cell mass; however, exercise that is too intense has the potential to cause red cell destruction (63).

The correlation between the change in red cell mass and the change in VO_2max is low in short- and moderate-duration bed rest studies (31), and changes in aerobic capacity can be observed during short-duration bed rest studies even without a measurable change in red cell mass (41). In general, hematocrit does not change during bed rest, suggesting that the oxygen carrying capacity per unit of blood is unchanged (31;43). However, as red cell mass continues to decline with longer bed rest, albeit at a slower rate (134), the total oxygen delivery capacity of the blood is reduced at rest and during submaximal exercise (58) and further impaired at maximal exercise when maximal Qc also is reduced (57). Capelli et al. (23) reported that hemoglobin concentration was decreased by 9% after 42 days of bed rest, which along with the decrease in Qc was reflected in a 34% decrease in total oxygen delivery. However, arterial saturation of hemoglobin was unchanged during bed rest (23;57).

E. Contributing Factors to Decreased Aerobic Capacity

1. Orthostatic Stress

The influence of gravity on work performance is apparent when comparing results from supine versus upright exercise capacity after equal durations of simulated microgravity. After short duration bed rest, VO_2max decreased 2-2.5 times more during upright exercise compared to supine exercise (26;38). After 10 days of bed rest in middle-aged men, the reduction in VO_2max was 15% in the upright posture, but was only 6% (N.S.) when subjects were tested in the supine posture (26). Submaximal exercise responses are similarly affected; at the same absolute work intensity (115 Watts) pre- and post-bed rest, HR was elevated by 4% above pre-bed rest values when subjects performed supine ergometry, but was increased by 8% when the exercise was performed upright. Exercise in the upright posture is associated with a greater reduction in SV and Qc than supine exercise. Saltin et al. (148) reported that both resting and exercise SVs were reduced to a greater extent when subjects were upright (Rest:-24%, Exercise: -35%) than when the subjects were supine (Rest: -17%, Exercise: -23%).

Exercise alone prevents the loss of aerobic capacity when pre- and post-bed rest tests are performed in the supine posture. Similarly, in-flight exercise capacity is maintained by in-flight exercise during short- and long-duration space flight when crewmembers are not exposed to orthostatic stress. However, the maintenance of upright exercise capacity is more relevant to Space Shuttle and ISS crewmembers who may be required to egress without assistance from the Shuttle in an emergency, or during exploration missions when work in an extravehicular suit in a partial gravity field, shortly after planetary landing, may be integral to mission success (101;184). Emergency egress from the Shuttle represents a significant metabolic (>2.5 $l \cdot min^{-1}$) and cardiovascular (>160 $beats \cdot min^{-1}$) stress in normal ambulatory subjects (15) and would be a much greater challenge after long-duration ISS missions that typically last six months or more.

A potential relationship between the preservation of orthostatic tolerance and exercise performance by implementation of a single countermeasure would be an attractive feature to NASA. During recent studies utilizing exercise and LBNP as an orthostatic stressor, the countermeasure subjects maintained aerobic capacity (104;105;156;184) and experienced smaller bed rest-induced changes in cardiovascular responses during subtolerance orthostatic stress (157) and attenuated orthostatic intolerance (186). Using these data to specifically link orthostatic tolerance and exercise capacity is weakened when relying upon these data sets alone because the countermeasure is a combination of exercise and orthostatic stress. However, data from Space Shuttle missions suggest that crewmembers who perform more exercise during space flight experience less change in aerobic capacity (67)and smaller increases in HR during standing (103).

2. Cerebral Perfusion

Inadequate cerebral perfusion during post-bed rest exercise also might impair exercise performance, particularly when performed against an orthostatic stress. Prior to 30 days of bed rest, the majority of subjects terminated graded exercise tests due to general fatigue and shortness of breath (104;105). After bed rest, half of the control subjects who performed no countermeasures reported lightheadedness or loss of balance as the primary reasons for test termination. In contrast, fatigue and shortness of breath remained the predominant symptoms at test termination after bed rest in a group of subjects who performed an exercise countermeasure which maintained VO_2max.

3. Submaximal Exercise Responses

Aerobic deconditioning after bed rest is evident by higher HR, ventilation, respiratory exchange ratio, and rating of perceived exertion during submaximal exercise (28;29;38;43;63;88;101;104;105;128;156;166;184). Of these, elevated HR during submaximal exercise is the most prominent feature of bed rest-induced deconditioning. Submaximal exercise HR was increased following 24 hours of bed rest by approximately 20 beats$\cdot$min^{-1}, which Nixon et al. (128) noted was similar to the increase observed in Apollo and Skylab astronauts following space flight. Similarly, submaximal exercise HR was increased in almost every stage during supine ergometry following 14 days of bed rest, whether subjects performed a moderate intensity exercise countermeasure or not (169). After 17 days of bed rest, submaximal HR at 150 Watts was significantly increased by the eighth day of bed rest and remained elevated throughout the first post-bed rest exercise test (178). However, when subjects perform a countermeasure which preserves aerobic exercise capacity, submaximal HR is unchanged from pre-bed rest levels (87;101;104;105;184).

Elevated submaximal exercise HR after bed rest likely is a compensatory mechanism to maintain Qc when SV is decreased. Following 20 days of bed rest, submaximal Qc was not different during upright exercise, although HR was increased and SV was reduced in subjects performing no countermeasures (87). HR increased and stroke was reduced when the subjects were at rest in both sedentary and endurance trained subjects following 3 days of bed rest. Although maximal SV and Qc were not measured, submaximal SV was reduced and HR was elevated only in sedentary subjects. The fact that no change was observed in endurance athletes might have been because the submaximal workloads (up to 150 W) represented a proportionally lower percentage of their maximal exercise capacity (Control: 188 W, Endurance: 270 W, Strength: 225 W) (166).

Elevated ventilation and respiratory exchange ratio may be related to a shift from fatty acids energy sources towards carbohydrates (87;101), as has been observed with normal ambulatory detraining (122;123), or to a bed rest-induced reduction in lactate threshold and/or a greater concentration of blood lactate during submaximal exercise (41;148;166;170;191). The effect of bed rest on the lactate threshold may be more apparent in more highly trained subjects, who also experience a decrease in the norepinephrine response threshold during graded exercise after short-duration bed rest (166). The impaired ability of skeletal muscle to utilize aerobic pathways after bed rest for energy utilization might be inferred from the loss of aerobic pathway enzymes (81) and reduced glucose transporter content (175), or to reduced or inappropriate distribution of blood flow, as has been observed in animal models during exercise (192). Also, the loss of buffering capacity related to a decrease in bicarbonate ions with a decrease in plasma volume and slower oxygen kinetics have been proposed to contribute to the reduction in lactate threshold. Lactate threshold is an indicator for changes in aerobic endurance capacity which may occur independently of changes in VO_2max (20), which could signal a potential for earlier onset of fatigue and impaired ability to perform sustained tasks.

4. Thermoregulation

Physical work capacity after bed rest and space flight may be further reduced by impaired body temperature regulation during rest and exercise that, in turn, may lead to heat strain and injury. With regard to space flight, the combined effects of plasma volume loss and loss of heat acclimation may result in excessive heat strain for crewmembers wearing protective garments during launch and landing (133). During a nominal landing (STS-90, April 1998) prior to exit from the Space Shuttle, intestinal temperature (core temperature) was significantly elevated in four crewmembers wearing the required Launch and Entry Suit (LES) despite the use of a liquid cooling garment (140). In the event of an emergency egress from the Shuttle, crewmembers would be disconnected from the thermoelectric cooling unit supplying the liquid cooling garment in order to exit the vehicle; and they would then be required to ambulate to a safe distance. This activity would be completed fully suited and may require an effort in excess of 70% of the crewmember's preflight VO_2max (15). The combined thermal load of the protective garment and the elevated metabolic rate during egress would be expected to rapidly increase core temperature.

Impaired thermoregulation at rest and during exercise is evident after bed rest. Crandall et al. (45) passively heated subjects with a warm water-perfused suit before and after 15 days of bed rest. After bed rest, these subjects had a reduced forearm blood flow and vascular conductance both before and during whole body heating as well as an elevated oral temperature threshold at which forearm vascular conductance increased in response to the heat stress. Michikami et al. (119), using similar techniques, also observed an increase in the threshold temperature and decreased sensitivity of the vascular conductance and sweating response following 14 days of bed rest. A higher core temperature has been observed during submaximal exercise in both warm (60) and temperate (74;106) conditions, with changes occurring in as little as 24 (55) to 72 hours (166). The elevated post-bed rest core temperature during exercise was ascribed to a decreased ability to increase skin blood flow (68;106) (**Figure 19**) but also may be related to impaired sweating responses (74;106). However, the performance of an exercise countermeasure during bed rest has been shown to prevent these deleterious adaptations (46;160). This exercise countermeasure protocol also was demonstrated to preserve aerobic capacity.

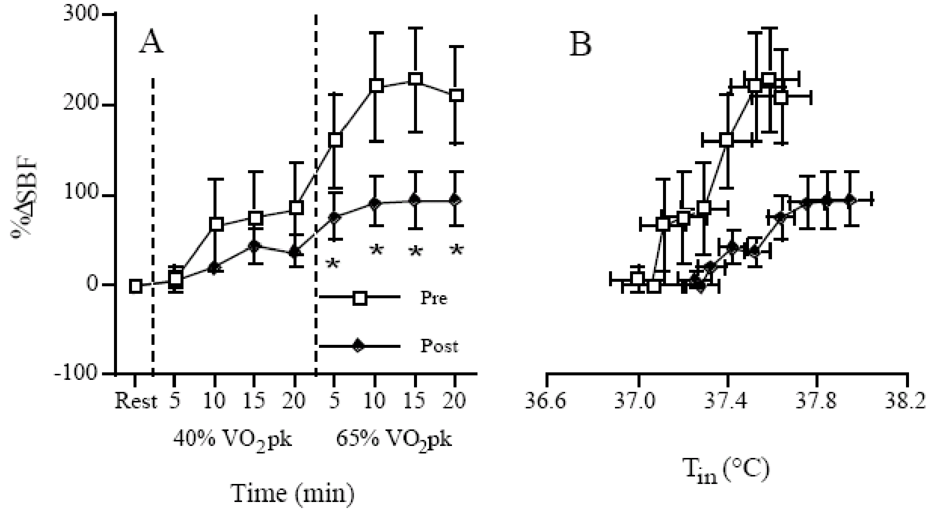

Figure 19. The change in skin blood flow in response to increasing core temperature during submaximal exercise is reduced after bed rest (Panel A). The onset of the vasodilatory response was delayed and the slope of the response tended to be reduced (Panel B) (106).

Changes in thermoregulatory control may be impacted during and after space flight. Leach et al. (99) reported that evaporative water loss was reduced by an average of 11% in 9 Skylab crewmembers during their in-flight exercise as compared to preflight. The authors suggested that the sweating responses may have been reduced in the microgravity environment through the formation of a film of sweat on the surface of the skin, because of reduced sweat dripping, which impaired air flow across the skin and sweat evaporation. Further, reduced gravity would have impaired spontaneous convection, in which air rises or falls due to differences in density (132), and low air flow in the cabin of space vehicles during space flight may limit heat loss capacity (61).

Fortney et al. (62) observed that the thermoregulatory mechanisms were severely impaired in two crewmembers when performing exercise following long-duration space flight (115 days) onboard the Mir space station. Both crewmembers had mildly elevated core temperature at rest and after 20 min of exercise at 40% VO_2max, and each had a delayed onset of and/or a decreased slope of sweating rate response and/or skin vasodilation. Neither crewmember was allowed to complete the second exercise stage postflight (20 minutes at 65% pre-flight VO_2max); the flight surgeon terminated the test "due to an excessive rise in HR." Despite the shortened exercise time, both crewmembers had a core temperature at the end of the postflight exercise bout similar to the core temperature at the end of the entire exercise protocol during pre-flight testing. Both crewmembers exhibited lower skin blood flow and sweating rate responses that may have contributed to this elevated core temperature.

F. Countermeasures

The optimal countermeasure prescription for the prevention of space flight-induced deconditioning should ideally include components to stimulate or maintain each organ system's condition similar to that maintained in a normal gravity environment (180), and it should require a minimal amount of crewmember time. The total time currently allowed for resistive and aerobic exercise on ISS, including set-up and stowage of the exercise hardware, and personal hygiene, is only 2.5 hours per day. Countermeasures that are too long or too intensive may reduce compliance in some crewmembers and may be difficult for schedulers to accommodate among various mission critical tasks (104). It is paramount that the countermeasures employed to protect crew health be of sufficient efficacy to promote and maintain high levels of function, such as aerobic and anaerobic fitness, in both male and female astronauts. As of 2001, 22% of the active astronaut corps was women (80), and the proportion of female astronauts may continue to increase. Care must be taken, however, when attempting to implement countermeasures that were successful in bed rest to the space flight environment due to logistical constraints of the space flight environment. In addition to crew time, exercise hardware mass, volume, and stowage should be considered as well as the impacts of countermeasure performance on the environmental control systems.

Although the preservation of aerobic capacity and exercise performance after short-duration bed rest studies primarily may be achieved through protecting against blood volume losses and changes in SV, the maintenance of exercise capacity during longer bed rest exposures also likely requires the maintenance of aerobic pathway enzymes (81), muscle strength and endurance, neuromuscular coordination, muscle capillary density, and cardiac mass and function (49;135). However, relative hypovolemia may exacerbate the effects of other bed rest-induced adaptations during upright exercise above that experienced during supine exercise because of the translocation of blood below the hydrostatic indifference point with the addition of orthostatic stress.

1. Exercise

Exercise is a natural modality to consider when developing countermeasures to the decrease in aerobic capacity during and after bed rest. Moderate intensities of aerobic exercise are not consistently effective to prevent the loss of aerobic capacity (174). Stremel et al. (169) were unable to prevent the decrease in aerobic capacity during two weeks of bed rest when subjects performed two 30-minute bouts of supine cycle ergometry daily at an exercise intensity of 68% of pre-bed rest VO_2max. However, Shibasaki et al. (160) maintained aerobic capacity in a longer bed rest study (18 vs. 14 days) by increasing the total exercise time from 60 to 90 minutes at 75% pre-bed rest HR. By extending the length of the exercise countermeasure, plasma volume also was maintained (-2%, NS), while it was significantly decreased (-12%) in the shorter study (169).

Short, intense bouts of exercise in ambulatory subjects are considered to be more effective than longer, less strenuous exercise in promoting changes in aerobic fitness in ambulatory subjects (187), and therefore are perhaps more likely to provide protection during bed rest. Greenleaf at al. used a near maximal (up to 90% of pre-bed rest VO_2max) interval exercise, two 30-minute bouts, 5 days per week during a 30-day bed rest, to prevent the loss of both exercise capacity (69) and plasma volume (-1%, NS) (75). Control subjects in this study experienced an average decrease in VO_2max of 18%, but the subjects experienced no change in exercise performance (+3%, NS). The success of this protocol in bed rest prompted NASA Astronaut Strength, Conditioning, and Rehabilitation Specialists to include this protocol in their exercise prescriptions for astronauts onboard the ISS (Mark Guilliams, personal communication), and similar exercise countermeasure protocols have been used successfully in bed rest studies by other investigators (87;101;104;105;184).

In an attempt to develop a more time efficient exercise countermeasure protocol, Convertino et al. (27) had subjects perform a maximal bout of supine cycle ergometry as a simulation of exercise in microgravity at the end of a 10-day bed rest. Although VO_2max measured during this supine ergometry test was significantly reduced from pre-bed rest (-5.6%), when subjects performed an upright treadmill test 3 hours later, they exhibited no change in treadmill VO_2max compared to the pre-bed rest measurement. However, a single bout of intense exercise 24 hours before resumption of normal ambulatory activities which normalizes plasma volume (control: -16%, exercise: -4%, NS) (37) and protects LBNP tolerance (53), does not prevent a decrease in aerobic capacity (52). It has been postulated that factors other than the exercise countermeasure, including readaptation to the upright posture (69), likely influenced the preservation of treadmill exercise capacity observed in the earlier study.

Decreased muscle strength and endurance associated with bed rest deconditioning (63;100;124;125;159) also likely affect maximal exercise performance, particularly during cycle ergometry testing when knee extensor muscles are greatly involved. For example, decreased local muscle fatigability in the calf muscles following 16 days of bed rest was correlated with a decrease in VO_2max among control subjects (52). However, few studies have directly assessed the use of a resistive exercise countermeasure to protect aerobic exercise capacity. Stremel et al. (169) reported that subjects who performed two 30-minute sessions of static leg extension exercise (21% MVC for one minute followed by one minute of rest) during a 14 day bed rest study experience a significant decrease in aerobic capacity (-4.8%), but the loss appeared to be attenuated compared to both control subjects (-12.3%) and those subjects who had performed a moderate intensity aerobic exercise countermeasure (-9.2%). Similarly, when subjects in a 30-day bed rest study performed two 30 minutes bouts of maximal isokinetic exercise (10 seconds of work, 50 seconds of rest,15 minutes per leg) supine VO_2max was not preserved (-9.1%) but the loss was half that experienced by the control subjects (-18.2%) (69). This partial preservation of aerobic capacity using resistive exercise alone suggests that muscle strength and endurance are significant contributors to aerobic exercise performance after bed rest. Additionally, other studies which have used aerobic exercise countermeasures to prevent the decreased VO_2max following bed rest demonstrated a protection of muscle performance (1;104;186).

2. Artificial Gravity

The concept that gravitational or gravitational-like stress alone will provide some protection against the decrease in aerobic capacity associated with bed rest is not new. In the 1960s, several reports were published which suggested that the amount of deconditioning associated with chair rest was less than that observed following strict bed rest (14;95;96). Later work demonstrated that exposure to a real or simulated orthostatic stress alone may attenuate the loss of upright aerobic capacity during short-duration, but perhaps not longer duration, bed rest studies. Four hours of quiet standing (180) or 3 hours of peripheral fluids shifts induced by a reverse pressure gradient garment (43) were partially effective in protecting exercise capacity during 4 and 15 days of bed rest, respectively. In contrast, subjects who were exposed to two 30-min sessions of centrifugation (+2Gz) daily during 4 days of bed rest or daily multiple bouts of LBNP (-35 mmHg) during one month of bed rest experienced a similar loss of upright aerobic capacity as control subjects (84;141). These findings suggest that long-duration or more frequent exposures to orthostatic stress alone are necessary to protect against decreased post-bed rest exercise capacity.

Recently, NASA completed a 21-day bed rest study in which 15 male subjects were assigned to serve as controls or to receive an artificial gravity countermeasure generated by a short radius human-rated centrifuge (Dr. Alan Moore, Unpublished Results). Countermeasure subjects were exposed to one hour of artificial gravity per day, with a load equivalent to +2.5 G_z at the feet. The subjects performed upright cycle ergometer tests to measure VO_2max before bed rest and on the first day of recovery. VO_2max was reduced by 10% in the control group, but was not significantly changed in the subjects who received the artificial gravity countermeasure (-6%, NS; Dr. Alan Moore, personal communication). Following bed rest, plasma volume was reduced (-9%) in both control and countermeasure subjects, and there were no differences between the groups (Dr. Michael Stenger, Unpublished Results). However, the knee and ankle extensor muscle strength of the countermeasure subjects was superior to that of the control subjects, perhaps because the countermeasure subjects performed short range of motion knee bends and heel raises during the centrifugation to protect against presyncope (21), which may have aided in the performance of cycle test after bed rest.

3. Combination Protocols

Protection against the loss of aerobic capacity after bed rest is probably most effective when the simulated or real upright posture is coupled with exercise. The combination of orthostatic stress and even mild exercise reduces the countermeasure time requirement in bed rest by one half to produce a similar benefit (180). The addition of a gravity-like stress during exercise training may be necessary to maintain upright exercise responses after space flight and bed rest (38). Supine exercise may maintain plasma volume (75), but a gravitational component, real or simulated, may be required to maintain venous return and SV during post-bed rest exercise.

Centrifugation to simulate an orthostatic stress during cycle exercise has been successfully employed to maintain upright exercise capacity (**Figure 20**) (87). Subjects who performed two 20-minute sessions of combined exercise and centrifugation on alternating days of 20 days of bed rest maintained upright exercise capacity (-9±7%, NS), while those who did not perform the countermeasure experienced a significant loss (-27±7%). Countermeasure subjects exercised first for 20 minutes with a 0.8-1.4 Gz load at the heart while pedaling the cycle ergometer with a constant exercise intensity of 60 Watts. A 10 minute rest period without exercise or centrifugation was then permitted before subjects began the second exercise session. Subjects experienced 0.3 g at heart level during this session and performed an interval exercise protocol similar to one which had been previously used to preserve upright exercise capacity during 14-days of bed rest (184). In addition to protecting VO_2max, cardiopulmonary responses to submaximal exercise, including HR and SV, were maintained in subjects performing exercise during centrifugation.

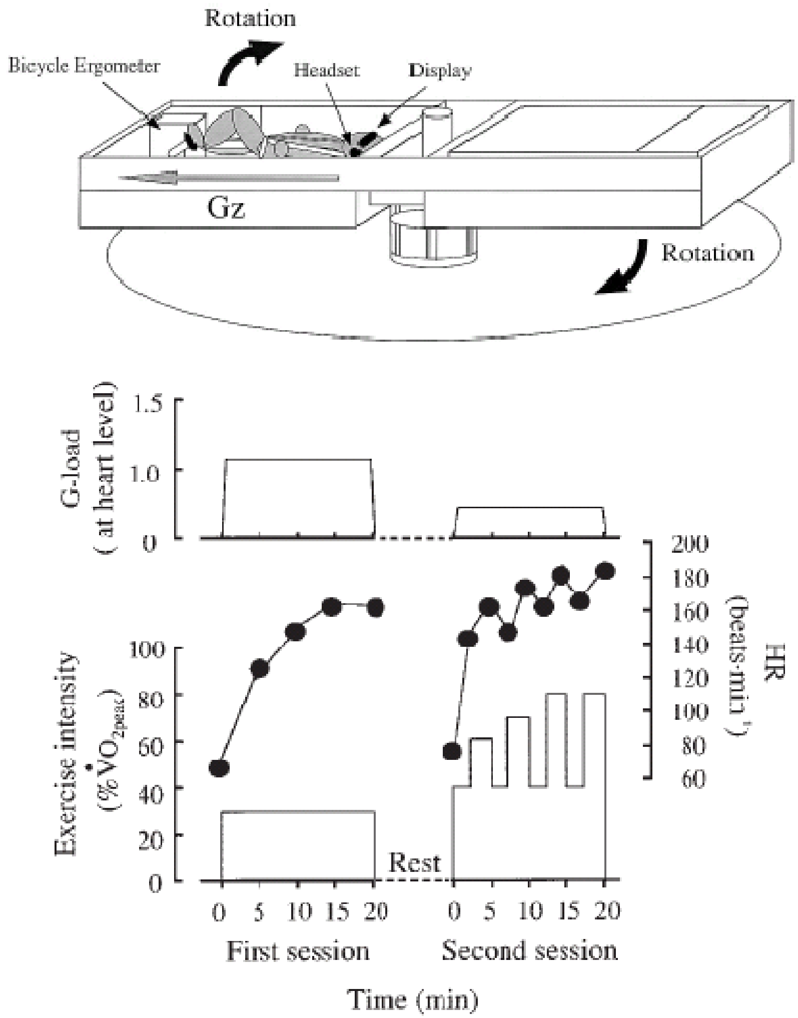

Figure 20. Centrifuge with cycle ergometer and the countermeasure protocol utilized by Katayama et al. (87) to preserve upright exercise capacity.

Technical and logistical barriers to continuous whole space craft rotation or intermittent short-radius centrifugation currently exist which make near term utilization of this centrifugation difficult, and therefore using lower body negative pressure (LBNP) to simulate orthostatic stress during an exercise may be an attractive alternative. The use of LBNP and exercise in separate sessions during bed rest was examined during a 28-day bed rest in which countermeasure subjects participated in a protocol of light supine cycle and isokinetic exercise throughout bed rest and LBNP (-40 mmHg for 15 minutes per day) in the latter half of a 28-day bed rest. Countermeasure subjects appeared to receive some protection against loss of aerobic capacity (-6% vs. Control: -16%), although the authors stated that this difference was “near the defined limit for statistical significance (p=0.06)” (82). Also, plasma volume was maintained in the countermeasure subjects but significantly reduced in the control group (112).

Concurrent treadmill exercise during LBNP (**Figure 21**) was developed over the past two decades (77-79) by a team of investigators led by Dr. Alan Hargens and Dr. Suzanne Schneider. The concept was developed in response to reports that long-duration crewmembers aboard the Mir space station exercise on the treadmill using loads equivalent to 60-70% of pre-flight body mass (188), which likely contributed to the inability of exercise countermeasures to fully prevent reduced aerobic capacity (120), bone loss (165), postflight orthostatic intolerance (116), and decreased muscle mass, strength, and endurance (108). Over the past decade the investigator team has documented the safety and effectiveness of a combined LBNP and treadmill exercise countermeasure. This integrated countermeasure method combines high loads on the musculoskeletal system with upright, Earth-like distributions of transmural pressure across blood vessels (78). Subjects participating in these studies have comfortably run on the treadmill for up to 40 minutes daily at up to 1.2 body weights (~60 mm Hg) and experience dynamic loading with inertial forces on the musculoskeletal and cardiovascular systems similar to those present during upright exercise on Earth (126;127). In fact, metabolic and biomechanical responses of treadmill exercise within LBNP during simulated microgravity are comparable to metabolic and biomechanical responses of upright treadmill exercise on Earth (19). The LBNP and exercise countermeasure system has prevented reductions in aerobic capacity, altered submaximal exercise responses, and decreased sprint performance (101;104;105;156;184) during 5, 15, 30, and 60 days of bed rest.

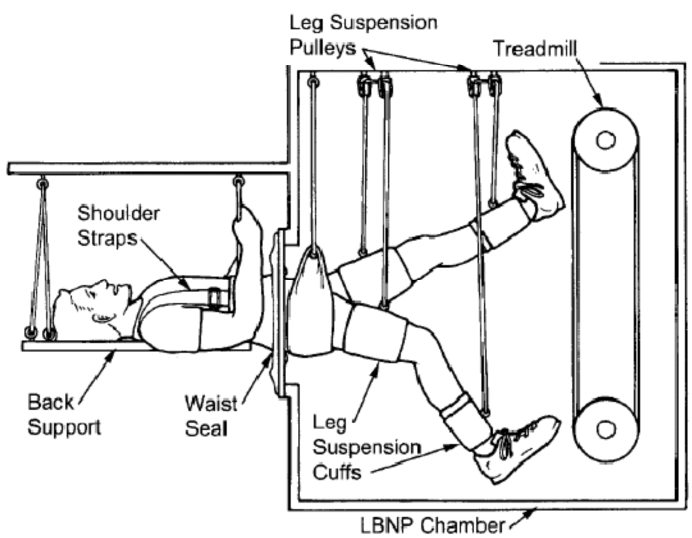

Figure 21. Illustration depicts the lower body negative pressure. This (LBNP) exercise device used for supine treadmill exercise during bed rest durations of 5, 15, 30, and 60 days (101;104;105;156;184). The device consists of a vacuum control system connected to a LBNP chamber enclosing a vertically oriented treadmill. A suspension system allowed subjects to perform treadmill exercise while supine by supporting their back and legs against the downward force of gravity. A broad, flexible neoprene waist seal spans the area between the subject and the edge of the elliptical opening. The waist seal area was to equal twice the subject's waist cross-sectional area, such that the negative pressure necessary to produce one body weight equaled -50 to -60 mmHg.

The LBNP and exercise device was first tested in a five-day bed rest study (101). Countermeasure subjects performed an interval exercise protocol which was modeled after one which successfully prevented a decrease in supine aerobic capacity (69) and protected plasma volume (75) during 30 days of bed rest. The LBNP and exercise subjects exercised daily for 30 minutes against LBNP which provided one body weight of loading (mean: -51 mmHg). After the exercise, both the upright and LBNP and exercise subjects stood (LBNP and exercise subjects experienced LBNP without exercise) for 5 minutes. The length of the bed rest was insufficient to observe a consistent change in upright VO_2max in the control group, but the submaximal exercise HR, respiratory exchange ratio, and ventilation were elevated. These changes during submaximal exercise were not evident in the LBNP and exercise group. LBNP and exercise training also prevented a decrease in plasma volume, which was observed in the control group, and protected against a decrease in tolerance to 30 minutes of head-up tilt (185).

The LBNP and exercise countermeasure was tested again during 15-days of bed rest in seven subjects using a cross-over design (184). The exercise protocol was modified by increasing the duration of the high work stages (3 vs. 2 minutes) and the total exercise time (40 vs. 30 minutes), but the target intensities were somewhat less than in the 5-day study (peak intensity 80% vs. 90% pre-bed rest VO_2max). The post-exercise LBNP exposure was not utilized in this project, but the amount of loading provided by LBNP was increased during the study to subject tolerance (1.0-1.2 body weight). When serving as controls, subjects experienced a significant decrease in aerobic capacity (-14%), but had no significant change in aerobic capacity after bed rest when they performed the LBNP and exercise countermeasure 6 days per week (-5%; **Figure 22**). Muscle performance also appeared to have been protected by this countermeasures; the time required to sprint 27.4 meters and plantarflexor muscle strength were maintained in the countermeasure subjects, while sprint time increased and plantarflexor strength decreased in the control condition. Additionally, the countermeasure attenuated the post-bed rest decrease in orthostatic tolerance, as measured using a progressive LBNP protocol, compared to the losses experienced by the control subjects (157).

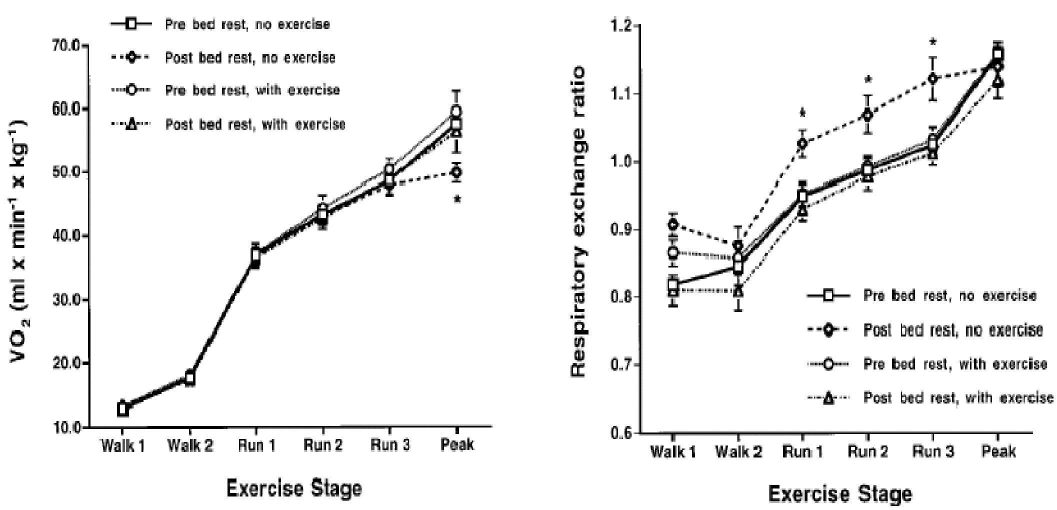

Figure 22. Submaximal and maximal oxygen consumption (VO_2) and respiratory exchange ratio before and after 15 days of bed rest with and without an LBNP and exercise countermeasure (from Watenpaugh et al. (184)

The LBNP and exercise countermeasure was later tested in male and female twins, one serving as the control and the sibling serving as the countermeasure subject, during 30 days of bed rest (104;105). The countermeasure protocol was the same as used in the

15-day bed rest study (184), except that the post-exercise LBNP exposure utilized in the 5-day study (101) was reinstated (**Figure 23**); the investigative team hypothesized that the post-exercise orthostatic stress when the skin and muscle bed were near maximally dilated were helpful in preserving orthostatic tolerance (157;186). Aerobic capacity was decreased in the control subjects after bed rest (-18%), but not in the LBNP and exercise subjects. The time required to sprint 30.5 meters (104;105)and knee, ankle, and trunk extensor muscle strength also were maintained in the countermeasure subjects, but not in the controls (22;154), Performance of the LBNP and exercise countermeasure protocol also attenuated the decrease in orthostatic tolerance (186). During head-up-tilt at sub-tolerance levels of orthostatic stress, SV and HR during head-up tilt were maintained after 30 days of bed rest in the countermeasures subjects.

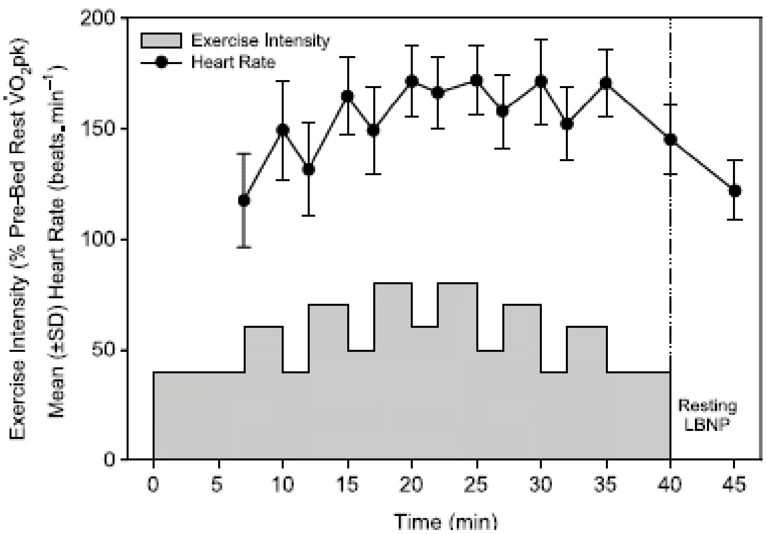

Figure 23. Mean HR response to the exercise countermeasure sessions performed by the male countermeasure (exercise plus LBNP) subjects during 30 days of bed rest (from Lee et al. (104).

Most recently, the LBNP and exercise countermeasure was tested during 60 days of bed rest (WISE-2005: Women's International Space Simulation for Exploration), in which countermeasure subjects also performed a resistive exercise protocol. Countermeasure subjects performed the LBNP and exercise protocol an average of 3 days per week and performed supine leg press and calf press on alternate days. The same exercise protocol as in the 15- (184) and 30-day bed rest studies (104;105) was utilized during LBNP and exercise sessions, but the duration of the post-exercise LBNP stress was increased to 10 minutes. The resistive exercise protocol was fashioned after a countermeasure protocol which was successful in preserving muscle strength and volume in male subjects during 29 and 90 days of bed rest (3;4). During a treadmill walking test on the first day of recovery, submaximal exercise responses were preserved in the countermeasure subjects but were elevated in the controls. When a maximal treadmill exercise test was conducted on the third day of recovery, VO_2max in the countermeasure subjects was not different than pre-bed rest (-3%, NS), although VO_2max was significantly decreased in the control subjects (-21%) (156). Unlike previous work, sprint performance was not tested in this study, but ventilatory threshold was determined to be preserved in the countermeasure subjects and decreased in the controls. Knee extensor muscle strength and endurance (109) and ankle extensor strength (179) also was preserved with this countermeasure. Additionally, LBNPex plus resistive exercise prevented cardiac atrophy in women during a 60-day bed rest (49). Left ventricular volume and long axis length was maintained in the countermeasure subjects during bed rest, and left ventricular mass, right ventricular mass, and mean wall thickness increased in these subjects.

Unfortunately, presumably due to the large budgetary requirements of performing bed rest studies with multiple groups, none of the investigations which have used a countermeasure combining orthostatic stress and exercise have utilized either a group who were exposed to orthostatic stress alone or exercise alone. Consequently, it is impossible to determine the proportional contributions of the countermeasure components, exercise alone, orthostatic stress alone, or their combination, on post-bed rest exercise performance.

Cycle ergometry and treadmill exercise have been the modalities of choice in studies which have combined exercise and simulated orthostatic stress, but it is not clear at this time which modality is most efficacious. Integration of cycle ergometry and artificial gravity within the confines of a space vehicle have been proposed (7;72;94). These centrifuge designs have included both the capacity for human-driven centrifugation to limit expenditure of spacecraft power and fuel as well as the capacity for passive riders. However, a human centrifuge has not been developed specifically as a countermeasure for long duration space flight perhaps because of difficulties related to vehicle integration (25).

Treadmill exercise may be a superior countermeasure to cycle ergometry as a means to prepare for emergency egress after landing on Earth and ambulation during EVA on the Moon and Mars. Treadmill exercise simulates many aspects of overground walking and running, and the countermeasure could be enhanced with the integration of a virtual environment (184). Additionally, treadmill exercise may prevent losses of bone mass and strength (164;196), and provides eccentric muscle actions which may efficiently counteract the loss of muscle strength (50;184). Other exercise modalities, such as stepping and squat exercise, have been proposed for use with centrifugation (193) and LBNP (183) but have not been tested in a bed rest model to determine their effectiveness to counteract the decrease in aerobic capacity.

G. Conclusions

The decrease in aerobic capacity during bed rest is rapid, occurring in a similar fashion as the loss of plasma volume during the first two weeks of bed rest. Thereafter, decreased VO_2max in response to bed rest progresses in a less steep rate of decay and is influenced by central and peripheral adaptation. Ferretti et al. (57) have suggested that following long-duration bed rest, 73% of the reduction in VO_2max can be explained by decreased oxygen transport from the lungs to the muscles, with the remaining influences equally divided between the oxygen diffusion and utilization at the cellular level. Bed rest investigations have demonstrated that frequent (at least 3 days per week), short bouts of intense exercise (interval-style and near maximal) during the bed rest period provides a time efficient level of protection against this form of cardiopulmonary deconditioning and also may safeguard against negative adaptations in other organ systems. Although exercise without orthostatic stress may be beneficial, complete protection against changes in upright exercise performance may be best realized when exercise is undertaken in combination with an orthostatic stressor as provided by centrifugation or LBNP.

IV. Computer-Based Simulation Information

As NASA plans for longer missions to the Moon and Mars, medical support personnel and mission planners need to anticipate the level of deconditioning that might be experienced during exploration mission and to allocate the required resources for countermeasure implementation. Because it is impractical to conduct all possible combinations of conditions (duration, crew composition, countermeasure type and availability, etc.) in space flight and bed rest studies, NASA instituted to Digital Astronaut Project. The Digital Astronaut Project is intended to develop a highly detailed model of the human body's physiologic systems and their integrated responses to the effects of space flight. In particular, modeling of the cardiovascular, pulmonary, and musculoskeletal systems may provide important clues regarding the effects of long duration exposures to micro- and partial gravity environments on work and exercise performance, with specific relation to the success of mission critical tasks.

Since VO_2max is primarily determined by Qc, we would expect any factors related to heart function or plasma fluid would be of functional significance. The impact of the microgravity induced changes in both plasma volume and diastolic function are integrated into the operation of the Digital Astronaut as noted in the graphic (Figure 24) below (24;171;172). The upper left hand curve in the panel describes the diastolic compliance of the left ventricle as it relates transmural pressures (TMP) to ventricular volumes. The lighter curve, as indicated by the arrow, depicts the shift in the compliance curve upon adaptation to the microgravity environment. This shift is due to the stiffness changes that occur with the fluid shifts in microgravity and a relative dehydration of the ventricular interstitial spaces. The stiffness of the left ventricle as a function of the interstitial fluid volume was described by Pogasta (136) and is shown in the curve in the lower part of the panel.

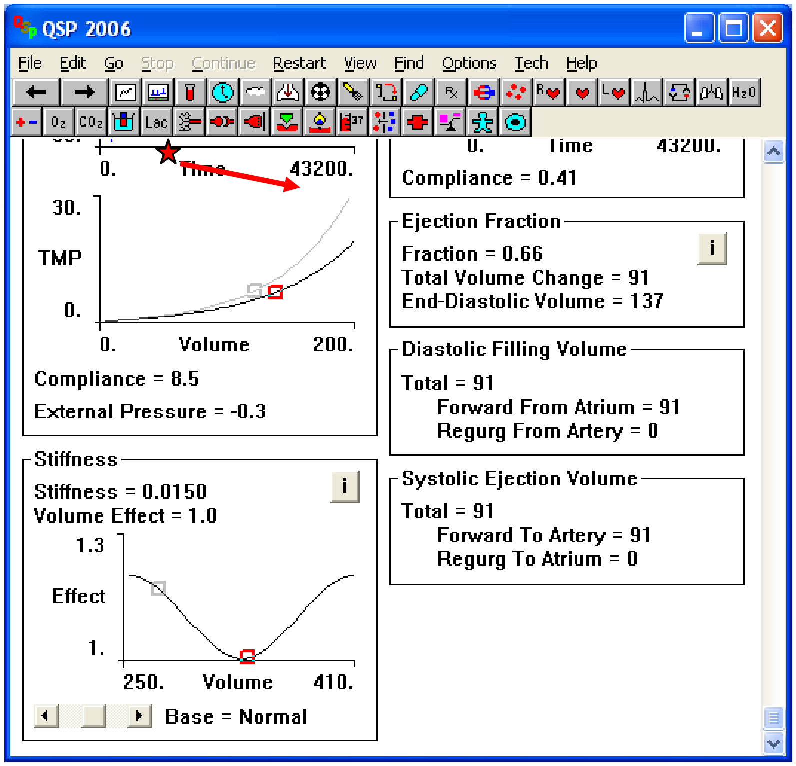

Figure 24. Simulation of microgravity effects on plasma volume and diastolic function.

Simulation studies using the Digital Astronaut Model replicate the findings demonstrated by Levine et al. of a 10% decrement in VO_2max upon reentry (111). This performance validation of the model predictions allows us to extrapolate to what might be expected for VO_2max changes immediately upon entering a Mars or lunar gravitational field (**Figures 25 and 26**).

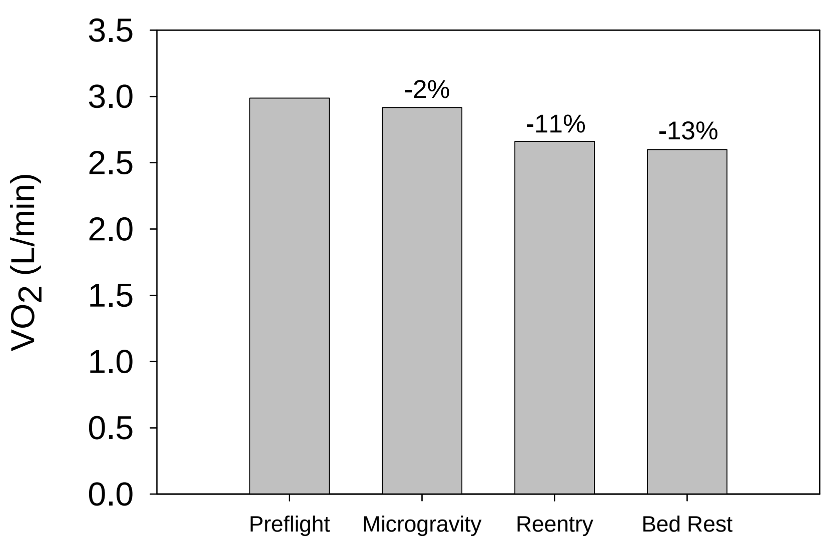

Figure 25. Simulation of the effects of space flight on VO_2max.

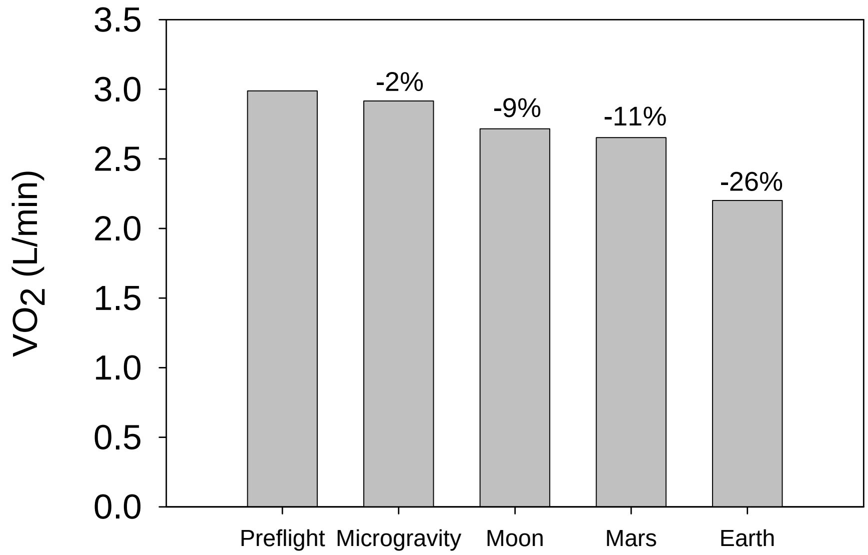

Figure 26. Model prediction of various gravity profiles on VO_2max.

V. Risk in Context of Exploration Mission Operational Scenarios

Astronauts must be physically prepared to perform any work that may be required for the safe, successful completion of mission tasks. Routine tasks on-orbit are not anticipated to require high levels of physical work, but astronauts also must have adequate reserves to act in and survive emergency conditions (42;71). During short duration flights, such as Space Shuttle missions, VO_2max does not decline sufficiently to impact normal onboard operations, but decreased functional capacity is apparent upon landing (111;121;178). Reduced physical capacity upon return to Earth may have a significant impact on a crewmember's ability to respond to an emergency situation or assist a crewmate who might be incapacitated. For example, performing the ambulation portion of an emergency egress simulation while wearing the NASA Launch and Entry suit requires a VO_2 of between 2.0 and 2.7 Liters $O_2 \cdot min^{-1}$, depending upon the amount of anti-gravity suit pressurization employed (15); this would be a maximal or near-maximal effort for many crewmembers immediately after a Space Shuttle mission (2.1-2.9 Liters $O_2 \cdot min^{-1}$, (121)).

EVA is a critical portion of space exploration and is performed by an astronaut working within a space suit. The EVA suit acts like personalized space craft with its own oxygen supply and carbon dioxide removal systems, micrometeorite and thermal protection, and radiation shielding. While these characteristics are desirable for autonomous operations separate from the Space Shuttle, *Soyuz*, ISS, or other vehicle, these capabilities come with a cost. Several factors associated with suit design, including internal suit pressure, suit mass and mobility, and heat removal capacity will impact an astronaut's ability to successfully complete a microgravity or planetary EVA.

The ability to perform physical work and activity is impeded because the astronaut must work against the suit's internal pressurization to manipulate tools, move equipment or perform construction tasks, and translate across the vehicle or planetary surface. The pressure differential between the suit environment and the vacuum of space is 4.3 psi (29.6 kPa) in the US EVA suit and 5.8 psi (40.0 kPa) in the Russian Orlan. Consequently, the amount of force that an astronaut can generate to manipulate tools and hardware and the amount of work that can be performed are reduced by 50% on average (66). The suit pressure could be reduced to minimize the resistance to movement and decrease the metabolic cost of EVA, but this would increase the risk of decompression sickness (64).

In a standard EVA, the astronaut can pace the work so that the metabolic cost is moderate. EVAs performed from the Space Shuttle and from the Russian *Mir* Space Station have elicited an average metabolic cost of ~ 200 $kcal \cdot hr^{-1}$ (~0.7 Liters $O_2 \cdot min^{-1}$) (71;89;181;182). This represents 20-30% of the average Shuttle astronaut's VO_2max measured during treadmill testing before flight (80). However, the majority of work during microgravity EVA is performed by the smaller muscle groups of the upper body; with the torso and lower body used primarily to adjust and maintain body position. VO_2max of the arms is approximately 70% of that which can be achieved by the legs; thus the average EVA would require approximately 30-45% upper body VO_2max over periods of 5 to 8 hours. More intense EVAs have been measured in the US EVA suit (500 $kcal \cdot hr^{-1}$, ~1.7 Liters $O_2 \cdot min^{-1}$) and peak work rates have achieved as much as 780 $kcal \cdot hr^{-1}$ (~2.7 Liters $O_2 \cdot min^{-1}$) in the Russian Orlan suit (71;89).

The total mass of the EVA suit is quite large in order to accommodate the equipment required to support all the necessary life support functions. The current US EVA suit for Space Shuttle and ISS operations weighs 133 kg on Earth, and the Russian Orlan suit weighs 112 kg. The large mass of the suits is not a significant issue during microgravity EVA as astronauts are not required to support the body and suit weight. In the 1/6-g environments of the Moon, the suit weight (Apollo: 100 kg) is expected to have a greater effect on EVA when astronauts are required to ambulate in the suit, manipulate tools and scientific equipment, and carry loads of rock samples, although some of the suit weight is supported by rigidity created by the internal suit pressure (153). Lunar EVA tasks involve more "whole body" work than microgravity-based EVAs, and the average metabolic cost of lunar EVA during Apollo (234 $kcal \cdot h^{-1}$, 0.8 L $O_2 \cdot min^{-1}$) was ~15% greater than microgravity EVA (181). Recent work at NASA Johnson Space Center, in which partial gravity ambulation is simulated using an unweighting system, has suggested that suit weight has a significant impact on metabolic rate across locomotion speeds (65).

The initial lunar EVA was performed by the crew of Apollo 11 in the evening of July 20, 1969, the first manned exploration of the moon's surface. This single EVA conducted by the Apollo 11 crew lasted only 2.5 h, but by the end of the Apollo program 14 EVAs were successfully completed, the longest of which lasted more than 7.5 h. During standard lunar EVA tasks, the highest metabolic rates associated with discrete tasks were recorded during overhead work, loading pallets and lunar samples, and drilling (181). Apollo EVAs were quite arduous in some tasks; and several EVAs were slowed by request of the monitoring flight surgeons as heart rates during the activities reached 150-160 $beats \bullet min^{-1}$ (138). During Apollo 11 and 12, all equipment and samples were hand-carried, which contributed to the metabolic cost of these EVAs. The use of a small equipment cart lowered the physical requirements of EVA during Apollo 14. During the Apollo 15-17 EVAs the use of a Lunar Rover Vehicle led to an increase in the distances traveled and explored, and there were decreases in the levels of physical work required and consumables used. There also were fewer reports of fatigue during these EVAs (190).

Clearly, the final EVA suit design and task requirements for Moon and Martian exploration will have a significant impact on the required level of physical fitness (VO_2max) for astronauts and cosmonauts. Assuming that there is no significant change to the current design of microgravity EVA suits which might be used during transit, the likelihood of microgravity EVA success is high. The transit to the Moon is short, and exercise countermeasures currently employed during longer missions appear to be adequate to support microgravity EVA readiness during the six-month transit to Mars. During the 15-year life of the Russian Mir Space station, 78 two-person EVAs were conducted by 36 crewmembers (89). Most EVAs were performed between 30 and 180 days of space flight, and some occurred as late as 304-350 days of space flight (90). As of ISS Expedition 18, there have been 104 EVAs conducted at the ISS, totaling 654 hours of EVA time. Of these, 35 were conducted by long duration members when the Space Shuttle was not docked to the ISS and were performed ranging from 32 and 165 days of flight [source: http://www.hq.nasa.gov/osf/EVA/EVA_totals_table.html].

The capability to maintain EVA performance during extended stays on the Moon and upon arrival at Mars is less clear. Apollo astronauts recently stated that exercise countermeasures are not necessary for short trips to the Moon (14 days or less) and felt that a preflight conditioning program would be adequate preparation for these missions (153). However, it is difficult to predict how an astronaut's physical fitness will change during extended lunar stays. Although NASA currently is developing a bed rest model to investigate this, there are no clear answers as to whether lunar gravity itself will provide any protection against decreased VO_2max without exercise in addition to EVA; the longest any of the Apollo astronauts spent on the moon was three days. Maintaining physical fitness during the transit to Mars should also be of concern. Crewmembers likely will be required to begin work soon after arrival on Mars and there will not be time for a long adaptation to Martian conditions (90). If adequate in-flight countermeasures are not available, due to lack of stowage or hardware failure, the astronauts' abilities to perform mission critical tasks may be impaired.

To determine the levels of cardiovascular exercise capacity, strength and countermeasure protection that will be required for EVA during these types of missions, a group of investigators in NASA's Johnson Space Center EVA Physiology, Systems, and Performance Project have initiated a series of projects to study the physiological, biomechanical, and subjective aspects of work and exercise in the partial gravity of the Moon and Mars. In the first of these studies, the metabolic cost of ambulation was measured while exercising on a treadmill in normal gravity, then during simulated Moon and Mars gravity. These trials were conducted under the following conditions: 1) unsuited, 2) exercising outside the suit but with the equivalent weighting of the subject plus the prototype exploration EVA suit (Mark III suit (55 kg), and 3) while wearing the Mark III (**Figure 27**) (65). The partial gravity of the Moon and Mars were simulated using a servo-controlled, pneumatic lift system with constant feedback from a strain gauge to provide near constant unloading.

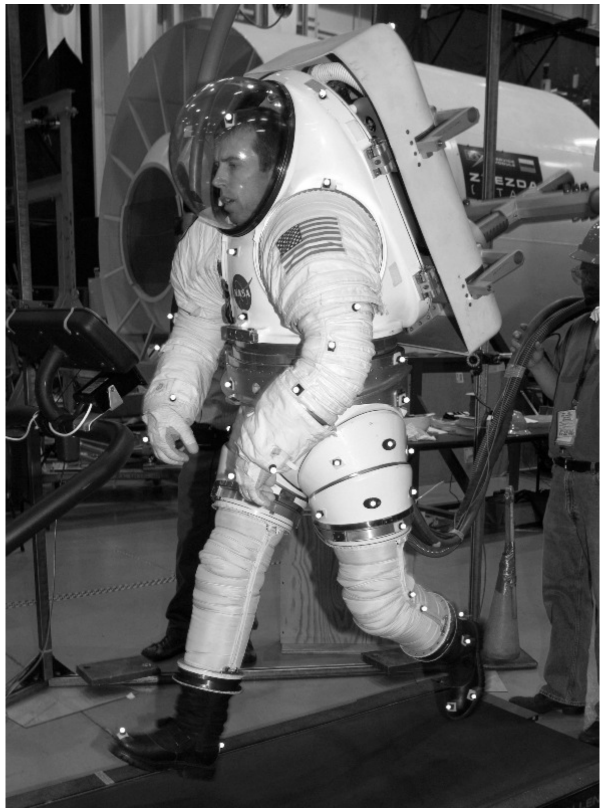

FIGURE 27. Astronaut performing treadmill walking in the Mark III prototype EVA suit.

The investigators reported that the metabolic cost of ambulation in simulated lunar and Martian gravity is substantially less than in normal gravity when unsuited. However, VO_2 increased by as much as 50% when the subjects were offloaded to reproduce the loading of the body weight plus the equivalent weight of the Mark III suit in partial gravity environments. At equivalent treadmill speeds, VO_2 in lunar gravity still was still less than VO_2 during normal gravity exercise without the suit weight; however, VO_2 in the Martian gravity simulation was not different than VO_2 in normal gravity. The effect of wearing the suit itself (i.e. mobility, internal pressurization, etc.), not just replicating the effects its weight, was evident. In the lunar simulations, wearing the Mark III increased VO_2 by an additional 7 $ml \cdot kg^{-1} \cdot min^{-1}$ (or ~20% of the subjects VO_2max) and in Martian simulations by an average of 20 $ml \cdot kg^{-1} \cdot min^{-1}$ (or ~40% of the subjects VO_2max).

During the later Apollo missions, the life support and consumables systems were upgraded to support an EVA >7 h in duration and the capability to walk 5 km back to the lunar habitat should the lunar rover fail (190). Current concepts for lunar surface operations and design for the next generation lunar rover propose that 10 km is an acceptable distance to cover in the EVA suit should the new rover fail while away from the lunar habitat (65). In light of this distance requirement, the NASA group investigated the feasibility of performing a 10 km traverse in simulated lunar gravity. Six experienced EVA crewmembers participated in the test and completed the walk while wearing the Mark III prototype suit. The astronauts performed the walk at a self-selected speed, which they were allowed to vary at any time, and averaged ~95 minutes to cover the distance. The average VO_2 measured during the task was ~2.0 L $O_2 \cdot min^{-1}$ (~50% of VO_2max) (64). The applicability of this work is limited by the fact that the test was conducted on a level treadmill with no obstacles to locomotion. Experience in lunar gravity has demonstrated the terrain features, particularly uphill walking, have a significant impact on VO_2 (181), an observation supported by later work using the lunar gravity simulation (64). Ground-based estimates suggest that, depending on the terrain, lunar surface VO_2 may be as much as 56% higher than that of level treadmill walking (131). The metabolic cost of "cross country" walking on the lunar and Martian terrain may be high and will require an above-average aerobic capacity to accomplish safely.

VI. Gaps

A. Unknown In-flight and Immediate Postflight VO_2max

It is necessary to document the changes in measured VO_2max and aerobic endurance during and following long duration spaceflight and lunar habitation missions. Related research questions include:

1) What exercise prescription (modality, frequency, intensity, duration) will be most effective to prevent decreases in aerobic capacity?

2) What is level of physical fitness, one component of which is measured by VO_2max, required to perform mission critical tasks, including emergency scenarios?

3) Does VO_2max interact with other factors of fitness (muscle strength, endurance, "anaerobic" threshold, orthostatic tolerance) to predict critical mission task success? Do we expect that other facets of physical fitness are more important predictors of mission success?

4) How much affect different levels of gravity will have on VO_2max upon reaching the Moon and Mars following microgravity exposure? How will this be mediated by inflight countermeasures?

5) What is the relative importance of different facets of physical deconditioning (e.g. plasma volume change, venous return, cardiac function, mitochondrial density and "aerobic" enzymes, control of blood flow) as they contribute to the decline in VO_2max as the duration of microgravity exposure continues? How will protection of one factor by countermeasures affect the contribution of other factors?

6) Will there be a protective effect of long-time exposure to partial gravity (such as 1/6 G on the Moon or 1/3-g on Mars) in comparison to exposure to microgravity?

VII. Conclusions

Aerobic capacity decreases following short-duration space flight and after bed rest, which is a space flight analogue. Although not directly measured, VO_2max is also believed to be reduced following long-duration space flight based upon observations of elevated HR responses to submaximal exercise loads. Reduced SV, perhaps secondary to lower plasma volume and decreased diastolic filling, is believed to be a major influence on exercise capacity, especially during orthostatic stress. Although no controlled studies of exercise countermeasure effectiveness have been conducted during space flight, data from bed rest studies have demonstrated that countermeasures may attenuate or completely protect aerobic capacity.

Whether exercise capacity is maintained during space flight is unclear, especially during long-duration missions. Understanding these changes is critical when designing a space flight mission and identifying the tasks that a crewmember will be expected to perform. Although performance of activities in microgravity has not been reported specifically to be impaired in space flight operations to date, decreased exercise capacity may decrease the efficiency and quality of work, the intensity at which a crewmember can work, and the duration for which the work can be performed. Crewmembers should maintain a level of fitness that provides additional reserve to be able to successfully react to emergency scenarios. Unfortunately, the required minimum level of fitness can not be fully defined until mission scenarios, critical mission tasks, and suit design are defined. However, acquiring the in-flight data, by direct measurement, that is necessary so planning is not based on assumptions about changes in VO_2max during and after space flight will assist in defining the problem more completely.

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